=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	199.75	373.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-29.25	-29.25

STN INTERNATIONAL LOGOFF AT 10:00:08 ON 12 JUN 2006

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FILE 'HOME' ENTERED AT 09:58:45 ON 12 JUN 2006

=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 09:58:52 ON 12 JUN 2006
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provided by InfoChem.

STRUCTURE FILE UPDATES:   11 JUN 2006  HIGHEST RN 887399-72-6
DICTIONARY FILE UPDATES:  11 JUN 2006  HIGHEST RN 887399-72-6

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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Uploading C:\Program Files\Stnexp\Queries\QUERIES\10719080.str
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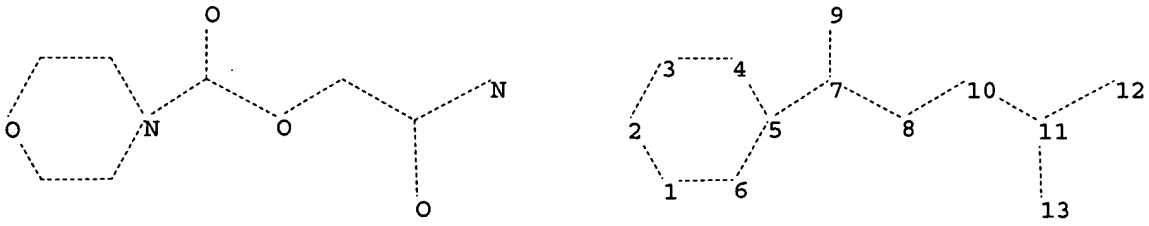


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chain nodes :
7  8  9  10  11  12  13
ring nodes :
1  2  3  4  5  6
chain bonds :
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ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
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PASSWORD:
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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  JAN 17   Pre-1988 INPI data added to MARPAT
 NEWS  4  FEB 21   STN AnaVist, Version 1.1, lets you share your STN AnaVist
                   visualization results
 NEWS  5  FEB 22   The IPC thesaurus added to additional patent databases on STN
 NEWS  6  FEB 22   Updates in EPFULL; IPC 8 enhancements added
 NEWS  7  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS  8  MAR 03   Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS  9  MAR 22   EMBASE is now updated on a daily basis
 NEWS 10  APR 03   New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 11  APR 03   Bibliographic data updates resume; new IPC 8 fields and IPC
                   thesaurus added in PCTFULL
 NEWS 12  APR 04   STN AnaVist $500 visualization usage credit offered
 NEWS 13  APR 12   LINSPEC, learning database for INSPEC, reloaded and enhanced
 NEWS 14  APR 12   Improved structure highlighting in FQHIT and QHIT display
                   in MARPAT
 NEWS 15  APR 12   Derwent World Patents Index to be reloaded and enhanced during
                   second quarter; strategies may be affected
 NEWS 16  MAY 10   CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS 17  MAY 11   KOREAPAT updates resume
 NEWS 18  MAY 19   Derwent World Patents Index to be reloaded and enhanced
 NEWS 19  MAY 30   IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS 20  MAY 30   The F-Term thesaurus is now available in CA/CAplus
 NEWS 21  JUN 02   The first reclassification of IPC codes now complete in
                   INPADOC

 NEWS EXPRESS      FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
                   CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
                   AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
                   V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
                   http://download.cas.org/express/v8.0-Discover/

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *
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1-2  1-6  2-3  3-4  4-5  5-6  5-7  7-8  7-9  8-10  10-11  11-12  11-13

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS
 11:CLASS  12:CLASS  13:CLASS



L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1                STR
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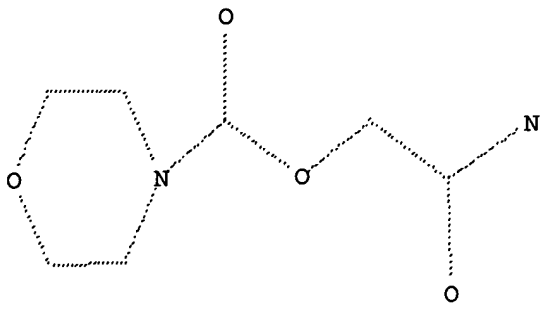


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Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SCREEN SEARCH COMPLETED -       22 TO ITERATE

100.0% PROCESSED       22 ITERATIONS                                 8 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          159 TO      721
PROJECTED ANSWERS:               8 TO      329

L2             8 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 09:59:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      417 TO ITERATE

100.0% PROCESSED      417 ITERATIONS                               192 ANSWERS
SEARCH TIME: 00.00.01

L3           192 SEA SSS FUL L1

=> s l3 and caplus/lc
      50991138 CAPLUS/LC
L4           191 L3 AND CAPLUS/LC

=> s l3 not l4
L5             1 L3 NOT L4

=> d
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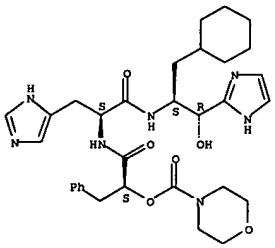
L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 734504-70-2 REGISTRY
ED Entered STN: 27 Aug 2004
CN 4-Morpholinecarboxylic acid,
2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-2-(1H-

imidazol-2-yl)ethyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-
oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*]]- (9CI) (CA INDEX
NAME)
FS STEREOSEARCH
MF C32 H43 N7 O6
CI COM
SR CA

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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=> fil caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       173.60     173.81

FILE 'CAPLUS' ENTERED AT 09:59:28 ON 12 JUN 2006
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FILE COVERS 1907 - 12 Jun 2006  VOL 144 ISS 25
FILE LAST UPDATED: 11 Jun 2006  (20060611/ED)

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=> s l4
L6          39 L4

=> d ibib abs hitstr 1-39
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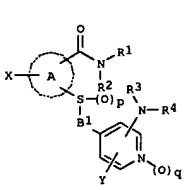
L6 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1004711 CAPLUS
DOCUMENT NUMBER: 143:286294
TITLE: Preparation of (pyridin-4-ylalkylthio)pyridine derivatives for treatment of diseases in which angiogenesis participates
INVENTOR(S): Honda, Takahiro; Tajima, Hisashi; Kawashima, Kenji; Okamoto, Kazuyoshi; Yamamoto, Minoru; Inaba, Takaaki; Takeno, Yuriko
PATENT ASSIGNEE(S): Santen Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085201	A1	20050915	WO 2005-JP2971	20050217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2006096739	A2	20060413	JP 2005-84772	20050217
PRIORITY APPLN. INFO.:			JP 2004-39862	A 20040217
			JP 2004-294347	A 20040906

OTHER SOURCE(S): MARPAT 143:286294
GI



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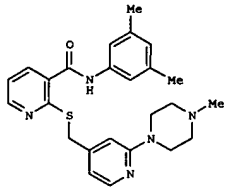
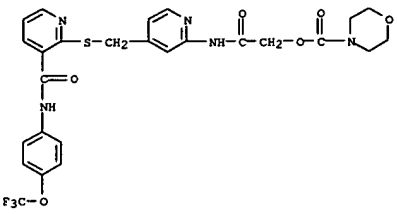


II

AB The title compds. I [wherein ring A = benzene, heterocycle, etc.; R1 and R2 = independently H, OH, alkoxy, etc.; R3 and R4 = independently H,

L6 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(un)substituted alkyl, etc.; X and Y = independently H, halo, OH, etc.; B1 = alkylene; p = 0-2; q = 0 or 1] or salts thereof were prepd. for the treatment of diseases in which angiogenesis participates. For example, the compd. II was prepd. in a multi-step synthesis in good yield. II inhibited 97% angiogenesis at the concn. of 20 μg/mL in cow. Some of compds. I showed good anticancer activity in rat. Formulations contg. I as an active ingredient were also described.
IT 864459-15-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of (pyridin-4-ylalkylthio)pyridine derivs. for treatment of diseases in which angiogenesis participates)
RN 864459-15-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-oxo-2-[[4-[[[3-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]-2-pyridinyl]thio]methyl]-2-pyridinyl]amino]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:395034 CAPLUS
DOCUMENT NUMBER: 142:430528
TITLE: Preparation of amino acid amides of 4-amino-5-hydroxytetrahydrofuran-2-one as inhibitors of cathepsin S
INVENTOR(S): Liu, Hong; Alper, Phillip B.; Mutnick, Daniel; Karanewsky, Donald S.
PATENT ASSIGNEE(S): IRM LLC, Bermuda
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

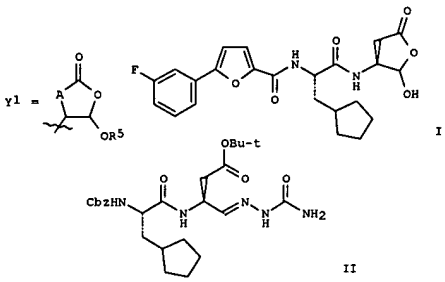
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005039496	A2	20050506	WO 2004-US35062	20041021
WO 2005039496	A3	20050915		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005130959	A1	20050616	US 2004-970344	20041020
PRIORITY APPLN. INFO.:			US 2003-513735P	P 20031021
			US 2004-970344	A 20041020

OTHER SOURCE(S): MARPAT 142:430528
GI

L6 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



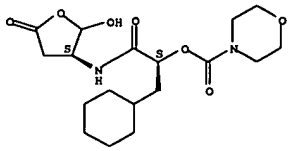
I

II

AB Title compds. YNHCOX [Y = CH(CHO)ACO2R5 or cyclic analog Y1; A = CH2, CH2CH2; R5 = H, C1-6 alkyl, C3-8 (substituted) cycloalkyl, CH2Ph; X = OCR1R2COQ, CHR3OCOW, CH2CHR3COW, CHR3CH2COW, CHR4NHCOW, OCR1R2BR6, CHR3HNHCO2Z, CHR4NHCOR7, CHR4NHSO2R8; Q = heterocycle such as pyrrolidinyl, piperidyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl substituted with 0-2 RQ; Q is connected to CO via a ring N atom; RQ = OH, SO2Me, COMe, :O, C1-6 alkyl, C1-6 alkoxy, CF3, OCF3, amines; W = morpholinyl connected to CO via ring N; Z = tetrahydrofuranyl, tetrahydropyranyl, thiotetrahydrofuranyl, thiotetrahydropyranyl, pyrrolidinyl, piperidyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, etc.; B = CH2, OCH2, NR11CH2, CH2CH2, a bond; R1 = H, (substituted) C1-6 alkyl, C2-6 alkenyl, C3-6 alkynyl, C3-7 cycloalkyl, C7-11 bicycloalkyl, (substituted) Ph, 5- to 6-membered heteroaryl, etc.; R2 = H, C1-6 alkyl; R3, R4 = (substituted) C1-2 alkyl; R6, R7, R8 = heteroaryl containing 1-4 heteroatoms each independently selected from N, O, S; R11 = H, C1-4 alkyl] were prepared as selective inhibitors of cathepsin S. For example, title compound I was prepared by coupling (3S)-amino-4-oxobutanoic acid t-Bu ester semicarbazone p-toluenesulfonate salt with Cbz-cyclopentylalanine dicyclohexylamine salt to give amide II, which was then deprotected of Cbz group and reacted with 5-(3-fluorophenyl)furan-2-carboxylic acid. The resulting product was deprotected and cyclized to give I. I showed selective inhibition of cathepsin S at <0.1 μM over cathepsins K and L. I inhibited caspases -1, -3 and -8 at >1 μM.
IT 850796-49-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and biol. activity of amino acid amides of tetrahydrofuranone derivs. as inhibitors of cathepsin S)
RN 850796-49-5 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-(cyclohexylmethyl)-2-oxo-2-[[(3S)-

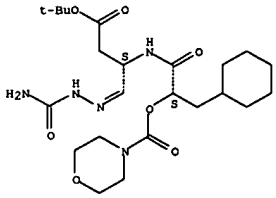
L6 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
tetrahydro-2-hydroxy-5-oxo-3-furanyl]amino]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **850796-85-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of amino acid amides of tetrahydrofuranone
derivs. as inhibitors of cathepsin S)
RN 850796-85-9 CAPLUS
CN 4-Morpholinecarboxylic acid,
(1S)-2-[[(1S)-1-[[(aminocarbonyl)hydrazono]methyl]-3-(1,1-dimethylethoxy)-3-oxopropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L6 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:346798 CAPLUS
DOCUMENT NUMBER: 142:369836
TITLE: Inhibitors of cathepsin S and pharmaceutical compositions containing cathepsin S inhibitors
INVENTOR(S): Liu, Hong; Chatterjee, Arnab; Tully, David C.; Alper, Phillip B.; Bursulaya, Badry; Guo, Jianhua; Woodmansee, David; Mutnick, Daniel; Karanewsky, Donald S.; He, Yun
PATENT ASSIGNEE(S): IRM LLC, Bermuda
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005034848	A2	20050421	WO 2004-US26986	20040819
WO 2005034848	A3	20051027		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005113356	A1	20050526	US 2004-922515	20040818
AU 2004279331	A1	20050421	AU 2004-279331	20040819
CA 2535930	AA	20050421	CA 2004-2535930	20040819
EP 1658267	A2	20060524	EP 2004-809589	20040819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.:
US 2003-496980P P 20030820
US 2004-922515 A 20040818
WO 2004-US26986 W 20040819

OTHER SOURCE(S): MARPAT 142:369836
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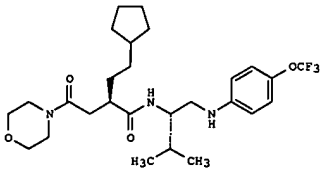
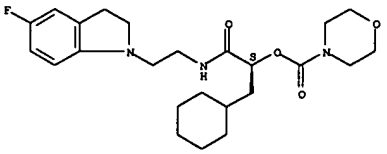
L6 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I

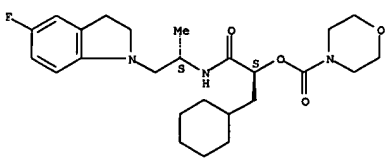
AB The present invention provides compds., compns. and methods for the selective inhibition of cathepsin S. In a preferred aspect, cathepsin S is selectively inhibited in the presence of at least one other cathepsin isoenzyme. The present invention also provides methods for treating a disease state in a subject by selectively inhibiting cathepsin S. Thus, 2-(R)-(2-cyclopentylethyl)-N-(2-methyl-1-(S)-[(4-trifluoromethoxyphenylamino)methyl]propyl)-4-morpholin-4-yl-4-oxobutyramide (I), along with numerous other similar compds., was synthesized. I exhibited a Ki for cathepsin S of <0.1μM and a selectivity for cathepsin S relative to cathepsins B, K, and L or >1000.
IT **849670-30-0P 849670-41-3P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of cathepsin S and pharmaceutical compns. containing cathepsin
S inhibitors)
RN 849670-30-0 CAPLUS
CN 4-Morpholinecarboxylic acid,
(1S)-1-(cyclohexylmethyl)-2-[[2-(5-fluoro-2,3-dihydro-1H-indol-1-yl)ethyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849670-41-3 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-(cyclohexylmethyl)-2-[[(1S)-2-(5-fluoro-2,3-dihydro-1H-indol-1-yl)-1-methylethyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



L6 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:417609 CAPLUS
DOCUMENT NUMBER: 139:958
TITLE: Aminodiols useful in the treatment of Alzheimer's disease and similar diseases
INVENTOR(S): Schostarez, Heinrich J.; Hanson, Gunnar J.
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
SOURCE: PCT Int. Appl., 535 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003043618	A2	20030530	WO 2002-US37180	20021119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2467476	AA	20030530	CA 2002-2467476	20021119
AU 2002352811	A1	20030610	AU 2002-352811	20021119
EP 1448177	A1	20040825	EP 2002-789765	20021119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014297	A	20041109	BR 2002-14297	20021119
US 2005080141	A1	20050414	US 2003-496091	20021119
JP 2005519874	T2	20050707	JP 2003-545299	20021119
PRIORITY APPLN. INFO.:			US 2001-332863P P	20011119
			WO 2002-US37180 W	20021119

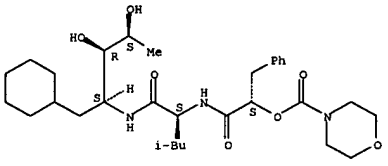
OTHER SOURCE(S): MARPAT 139:958

AB The invention discloses aminodiol compds. which modulate the activity of β-amyloid-converting enzyme for the treatment of Alzheimer's disease and similar diseases.

IT **120729-15-9 122621-75-4 122621-76-5 122994-22-3 122994-23-4 122994-25-6 533916-79-9 533916-80-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aminodiols for treatment of Alzheimer's disease)

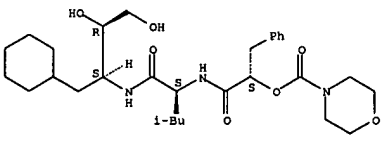
RN 120729-15-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



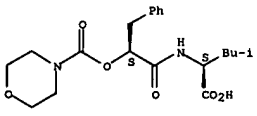
RN 122994-23-4 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R)-1-(cyclohexylmethyl)-2,3-dihydroxypropyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 122994-25-6 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-carboxy-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

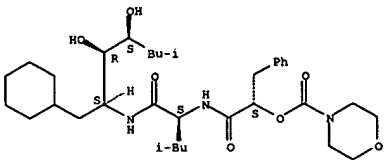
Absolute stereochemistry.



RN 533916-79-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[(2-carboxypropyl)amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

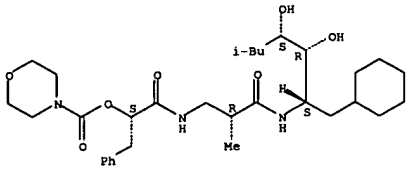
Absolute stereochemistry.

L6 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



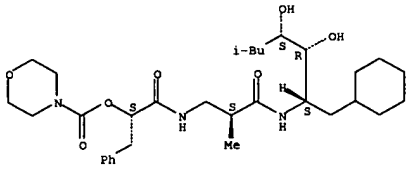
RN 122621-75-4 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(2R)-3-[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-2-methyl-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



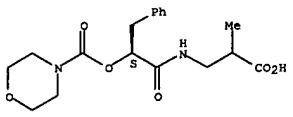
RN 122621-76-5 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(2S)-3-[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-2-methyl-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



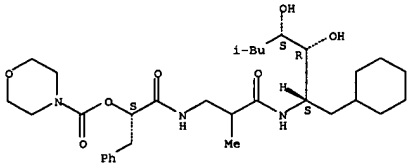
RN 122994-22-3 CAPLUS
CN L-Arabinitol, 1-cyclohexyl-1,2,5-trideoxy-2-[[(2S)-4-methyl-2-[[(2S)-2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]amino]-1-oxopentyl]amino]-

L6 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 533916-80-2 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[3-[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-2-methyl-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:964345 CAPLUS
DOCUMENT NUMBER: 138:24952
TITLE: Preparation of novel amino nitriles useful as reversible inhibitors of cysteine proteases
INVENTOR(S): Hickey, Eugene R.; Bekkali, Younes; Patel, Usha R.; Spero, Denice M.; Thomson, David S.; Young, Erick R. R.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

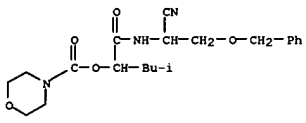
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100849	A2	20021219	WO 2002-US17590	20020605
WO 2002100849	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003119827	A1	20030626	US 2002-163015	20020604
US 6982263	B2	20060103		
CA 2449192	AA	20021219	CA 2002-2449192	20020605
EP 1399431	A2	20040324	EP 2002-741825	20020605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005501017	T2	20050113	JP 2003-503617	20020605
PRIORITY APPLN. INFO.:			US 2001-296863P P	20010608
			WO 2002-US17590 W	20020605

OTHER SOURCE(S): MARPAT 138:24952

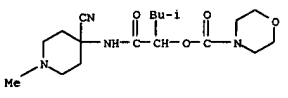
AB Novel nitrile compds. YCO2CR2R3C(:X)NR6CR4R5CN [Y = R1, R1O, R1S, R12N, R13C, where R1 = H, (un)substituted (cyclo)alkyl, aryl, benzyl, tetrahydronaphthyl, indenyl, indanyl, alkylsulfonylalkyl, cycloalkylsulfonylalkyl, arylsulfonylalkyl, heterocyclyl, or heteroaryl; R2-R5 = H, (un)substituted (cyclo)alkyl, aryl, etc. or CR2R3 and CR4R5 may form rings; R6 = H, OH, or (cyclo)alkyl; X = O or S (with provisos)] or their pharmaceutically-acceptable derivs. were prepared as reversible inhibitors of cysteine proteases such as cathepsin K, S, F, L and B for treating diseases and pathol. conditions exacerbated by these proteases such as osteoporosis, rheumatoid arthritis, multiple sclerosis, asthma and other autoimmune diseases, Alzheimer's disease, and atherosclerosis. Thus, morpholine-4-carboxylic acid 1-[[(benzyloxymethyl)cyanomethyl]carbam oyl]-3-methylbutyl ester was prepared from N-(tert-butoxycarbonyl)-O-benzyl-L-serine, 2-Hydroxyisocaproic acid, and 4-morpholinecarbonyl chloride.

IT **478279-49-1P 478279-54-8P 478279-57-1P**

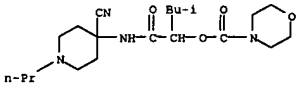
L6 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



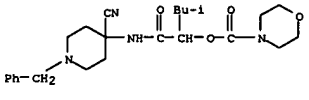
RN 478279-57-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)



RN 478279-58-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)



RN 478279-59-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[(4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)



RN 478279-60-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-cyano-1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

478279-58-2P 478279-59-3P 478279-60-6P
478279-61-7P 478279-62-8P 478279-94-6P
478279-96-8P 478279-97-9P 478279-98-0P
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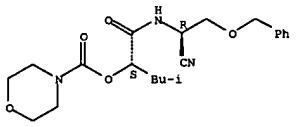
478281-80-0P 478281-81-1P 478281-82-2P
478281-83-3P 478281-84-4P 478281-85-5P
478281-86-6P 478281-87-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel amino nitriles as reversible inhibitors of cysteine proteases)

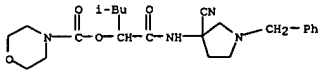
RN 478279-49-1 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



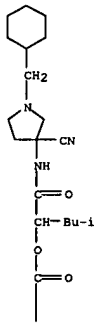
RN 478279-54-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 478279-61-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-cyano-1-(cyclohexylmethyl)-3-pyrrolidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

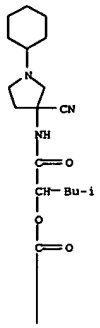
PAGE 1-A



PAGE 2-A

RN 478279-62-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[(3-cyano-1-cyclohexyl-3-pyrrolidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

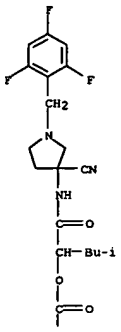
PAGE 1-A



PAGE 2-A

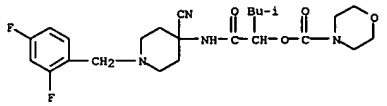
RN 478279-94-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-cyano-1-[(2,4,6-trifluorophenyl)methyl]-3-pyrrolidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

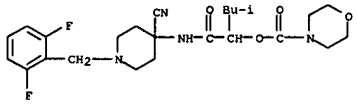


PAGE 2-A

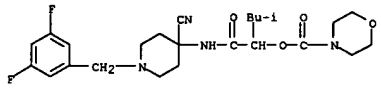
RN 478279-96-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[4-cyano-1-[(2,4-difluorophenyl)methyl]-4-piperidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)



RN 478279-97-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[4-cyano-1-[(2,6-difluorophenyl)methyl]-4-piperidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

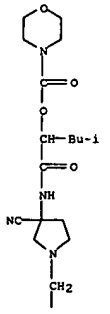


RN 478279-98-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[4-cyano-1-[(3,5-difluorophenyl)methyl]-4-piperidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

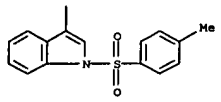


RN 478280-00-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-cyano-1-[[1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]methyl]-3-pyrrolidinyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

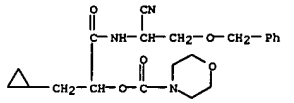
PAGE 1-A



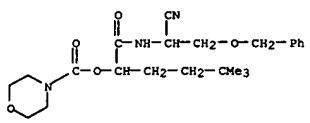
PAGE 2-A



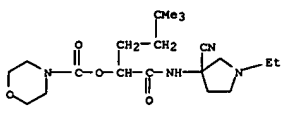
RN 478280-30-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclopropylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



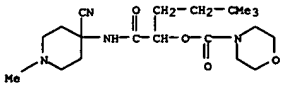
RN 478281-00-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-4,4-dimethylpentyl ester (9CI) (CA INDEX NAME)



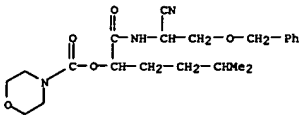
RN 478281-01-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-4,4-dimethylpentyl ester (9CI) (CA INDEX NAME)



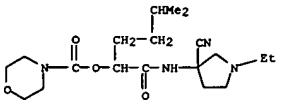
RN 478281-02-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl ester (9CI) (CA INDEX NAME)



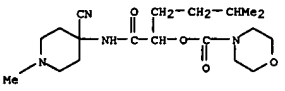
RN 478281-03-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-4-methylpentyl ester (9CI) (CA INDEX NAME)



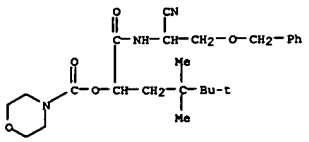
RN 478281-04-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-4-methylpentyl ester (9CI) (CA INDEX NAME)



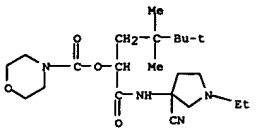
RN 478281-05-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4-methylpentyl ester (9CI) (CA INDEX NAME)



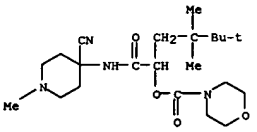
RN 478281-06-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3,4,4-tetramethylpentyl ester (9CI) (CA INDEX NAME)



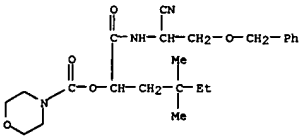
RN 478281-07-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl ester (9CI) (CA INDEX NAME)



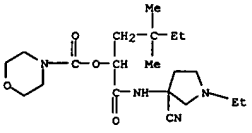
RN 478281-08-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl ester (9CI) (CA INDEX NAME)



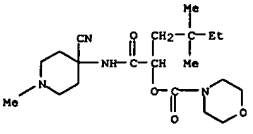
RN 478281-09-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylpentyl ester (9CI) (CA INDEX NAME)



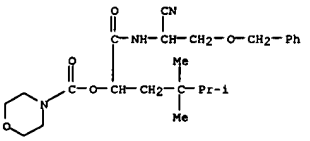
RN 478281-10-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3,3-dimethylpentyl ester (9CI) (CA INDEX NAME)



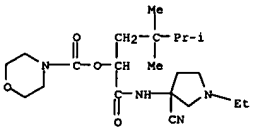
RN 478281-11-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylpentyl ester (9CI) (CA INDEX NAME)



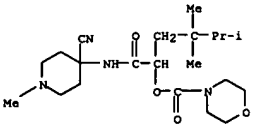
RN 478281-12-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3,4-trimethylpentyl ester (9CI) (CA INDEX NAME)



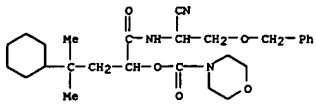
RN 478281-13-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3,3,4-trimethylpentyl ester (9CI) (CA INDEX NAME)



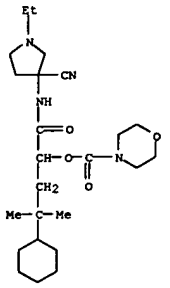
RN 478281-14-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3,3,4-trimethylpentyl ester (9CI) (CA INDEX NAME)



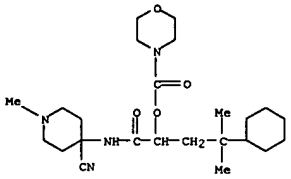
RN 478281-15-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-cyclohexyl-3-methylbutyl ester (9CI) (CA INDEX NAME)



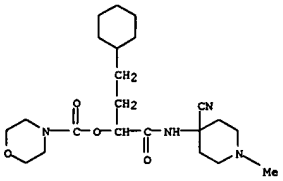
RN 478281-16-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3-cyclohexyl-3-methylbutyl ester (9CI) (CA INDEX NAME)



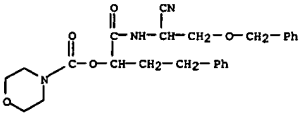
RN 478281-17-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3-cyclohexyl-3-methylbutyl ester (9CI) (CA INDEX NAME)



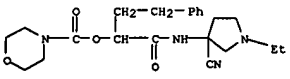
RN 478281-18-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]car



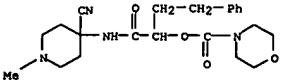
RN 478281-21-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-phenylpropyl ester (9CI) (CA INDEX NAME)



RN 478281-22-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3-phenylpropyl ester (9CI) (CA INDEX NAME)

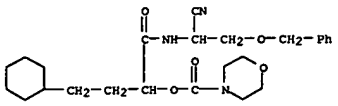


RN 478281-23-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3-phenylpropyl ester (9CI) (CA INDEX NAME)

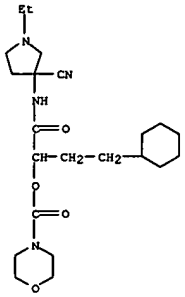


RN 478281-25-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

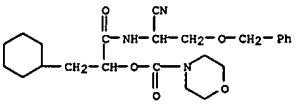
bonyl]-3-cyclohexylpropyl ester (9CI) (CA INDEX NAME)



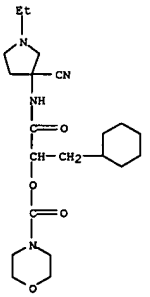
RN 478281-19-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3-cyclohexylpropyl ester (9CI) (CA INDEX NAME)



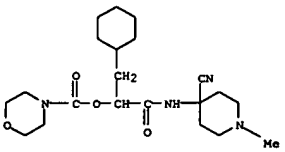
RN 478281-20-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3-cyclohexylpropyl ester (9CI) (CA INDEX NAME)



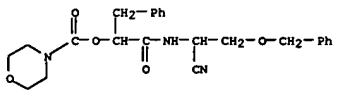
RN 478281-26-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



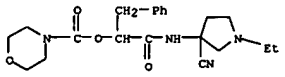
RN 478281-27-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



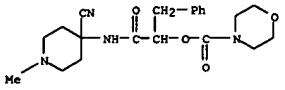
RN 478281-28-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(1-cyano-2-(phenylmethoxy)ethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)



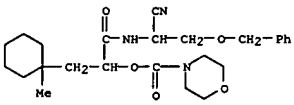
RN 478281-29-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)



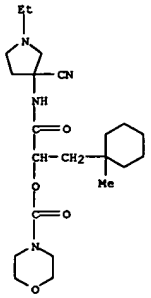
RN 478281-30-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)



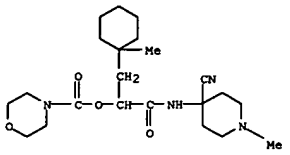
RN 478281-31-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(1-methylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



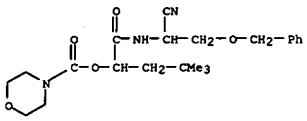
RN 478281-32-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(1-methylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



RN 478281-33-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(1-methylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

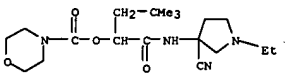


RN 478281-34-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylbutyl ester (9CI) (CA INDEX NAME)

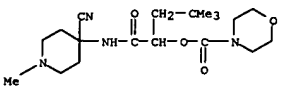


RN 478281-35-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-

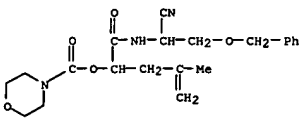
pyrrolidinyl)amino]carbonyl]-3,3-dimethylbutyl ester (9CI) (CA INDEX NAME)



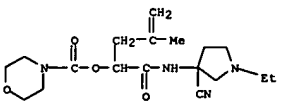
RN 478281-36-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl ester (9CI) (CA INDEX NAME)



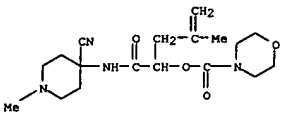
RN 478281-37-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methyl-3-butenyl ester (9CI) (CA INDEX NAME)



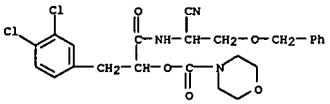
RN 478281-38-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3-methyl-3-butenyl ester (9CI) (CA INDEX NAME)



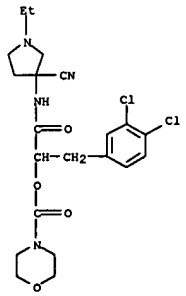
RN 478281-39-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3-methyl-3-butenyl ester (9CI) (CA INDEX NAME)



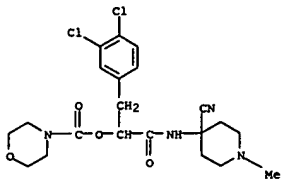
RN 478281-40-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(3,4-dichlorophenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



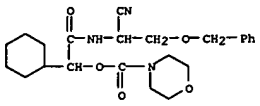
RN 478281-41-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(3,4-dichlorophenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



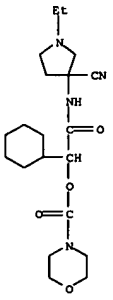
RN 478281-42-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(3,4-dichlorophenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



RN 478281-43-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-cyclohexyl-2-oxoethyl ester (9CI) (CA INDEX NAME)

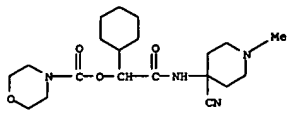


RN 478281-44-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-cyclohexyl-2-oxoethyl ester (9CI) (CA INDEX NAME)

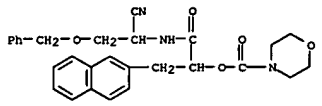


RN 478281-45-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-

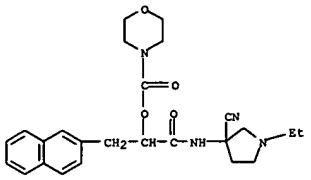
cyclohexyl-2-oxoethyl ester (9CI) (CA INDEX NAME)



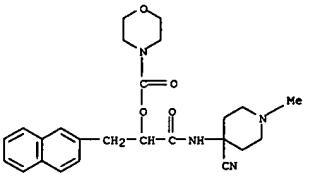
RN 478281-46-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



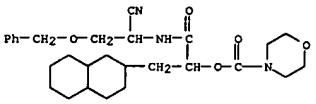
RN 478281-47-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-(2-naphthalenylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



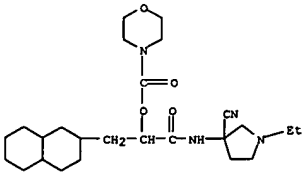
RN 478281-48-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(2-naphthalenylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



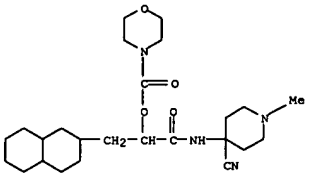
RN 478281-49-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(decahydro-2-naphthalenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



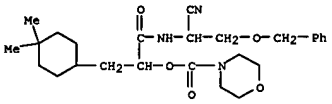
RN 478281-50-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(decahydro-2-naphthalenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



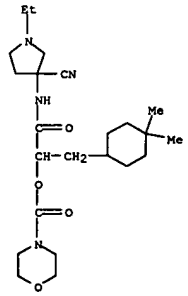
RN 478281-51-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(decahydro-2-naphthalenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



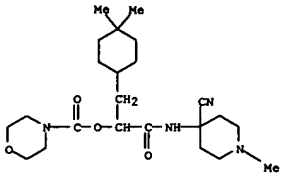
RN 478281-52-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(4,4-dimethylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



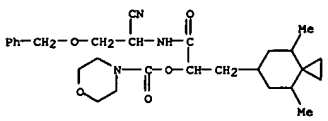
RN 478281-53-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(4,4-dimethylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



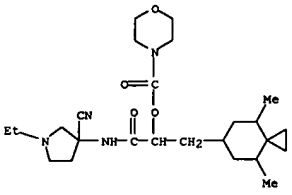
RN 478281-54-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(4,4-dimethylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



RN 478281-55-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(4,8-dimethylspiro[2.5]oct-6-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

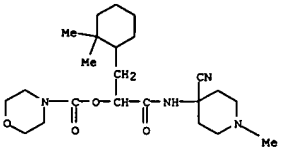


RN 478281-56-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(4,8-dimethylspiro[2.5]oct-6-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

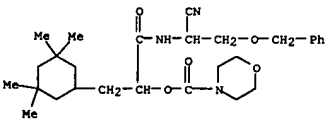


RN 478281-57-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(4,8-dimethylspiro[2.5]oct-6-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

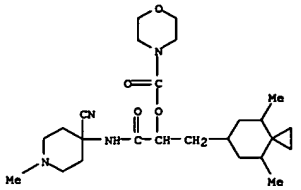
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(2,2-dimethylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



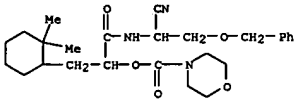
RN 478281-61-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-2-oxo-1-[(3,3,5,5-tetramethylcyclohexyl)methyl]ethyl ester (9CI) (CA INDEX NAME)



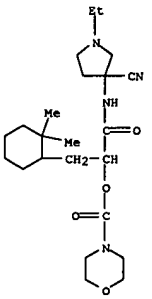
RN 478281-62-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-2-oxo-1-[(3,3,5,5-tetramethylcyclohexyl)methyl]ethyl ester (9CI) (CA INDEX NAME)



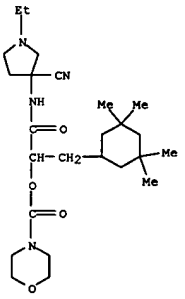
RN 478281-58-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(2,2-dimethylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



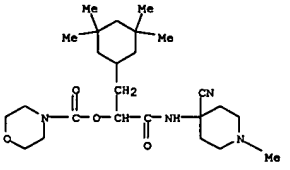
RN 478281-59-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(2,2-dimethylcyclohexyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



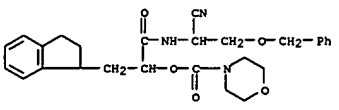
RN 478281-60-6 CAPLUS



RN 478281-63-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-2-oxo-1-[(3,3,5,5-tetramethylcyclohexyl)methyl]ethyl ester (9CI) (CA INDEX NAME)

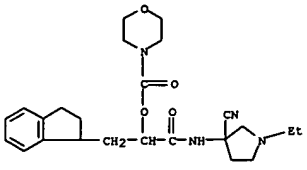


RN 478281-64-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(2,3-dihydro-1H-inden-1-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

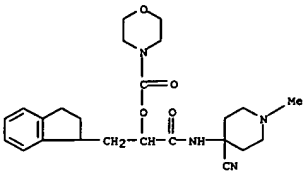


RN 478281-65-1 CAPLUS

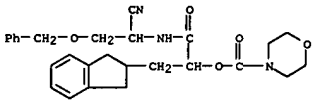
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(2,3-dihydro-1H-inden-1-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



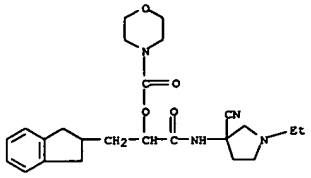
RN 478281-66-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(2,3-dihydro-1H-inden-1-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



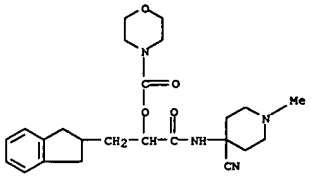
RN 478281-67-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(2,3-dihydro-1H-inden-2-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



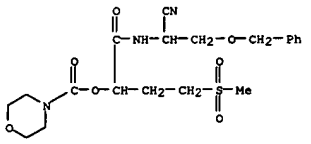
RN 478281-68-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(2,3-dihydro-1H-inden-2-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



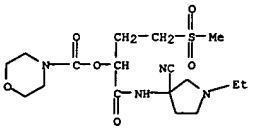
RN 478281-69-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(2,3-dihydro-1H-inden-2-yl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)



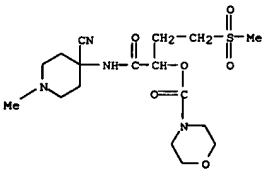
RN 478281-70-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-(methylsulfonyl)propyl ester (9CI) (CA INDEX NAME)



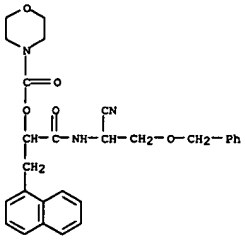
RN 478281-71-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3-(methylsulfonyl)propyl ester (9CI) (CA INDEX NAME)



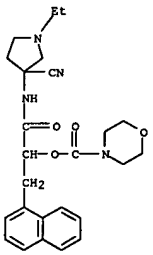
RN 478281-72-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3-(methylsulfonyl)propyl ester (9CI) (CA INDEX NAME)



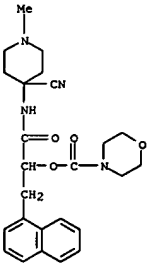
RN 478281-73-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(1-naphthalenylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



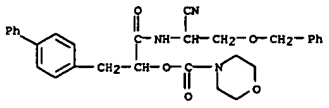
RN 478281-74-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-(1-naphthalenylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



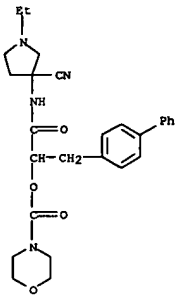
RN 478281-75-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(1-naphthalenylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)



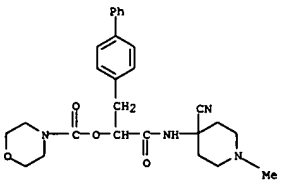
RN 478281-76-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-([1,1'-biphenyl]-4-ylmethyl)-2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

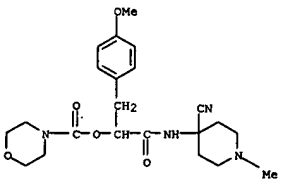


RN 478281-77-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-([1,1'-biphenyl]-4-ylmethyl)-2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

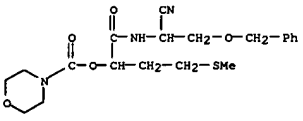


RN 478281-78-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-([1,1'-biphenyl]-4-ylmethyl)-2-[(4-cyano-1-methyl-4-piperidinyl)amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

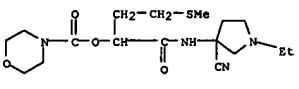




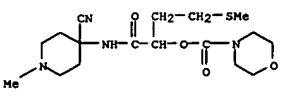
RN 478281-82-2 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-(methylthio)propyl ester (9CI) (CA INDEX NAME)



RN 478281-83-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-3-(methylthio)propyl ester (9CI) (CA INDEX NAME)

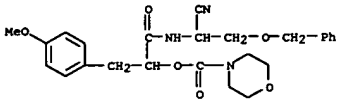


RN 478281-84-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3-(methylthio)propyl ester (9CI) (CA INDEX NAME)

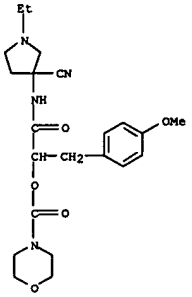


RN 478281-85-5 CAPLUS

RN 478281-79-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-cyano-2-(phenylmethoxy)ethyl]amino]-1-[(4-methoxyphenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

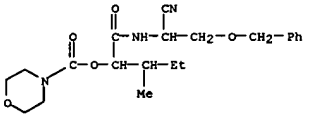


RN 478281-80-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]-1-[(4-methoxyphenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

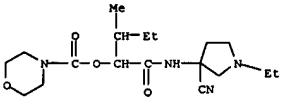


RN 478281-81-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[(4-methoxyphenyl)methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

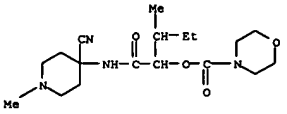
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-2-methylbutyl ester (9CI) (CA INDEX NAME)



RN 478281-86-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-ethyl-3-pyrrolidinyl)amino]carbonyl]-2-methylbutyl ester (9CI) (CA INDEX NAME)

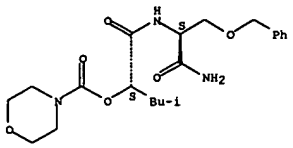


RN 478281-87-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-2-methylbutyl ester (9CI) (CA INDEX NAME)



IT 478279-48-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel amino nitriles as reversible inhibitors of cysteine proteases)
RN 478279-48-0 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-[[[(1S)-2-amino-2-oxo-1-[(phenylmethoxy)methyl]ethyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 2002:946262 CAPLUS
DOCUMENT NUMBER: 138:24946
TITLE: Preparation of amide compounds and compositions as selective cathepsin S inhibitors
INVENTOR(S): Graupe, Michael; Li, Jiayao; Link, John O.; Zipfel, Sheila; Timm, Andreas P.; Aldous, David J.; Thurairatnam, Sukanthini
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA; Aventis Pharmaceuticals Inc.
SOURCE: PCT Int. Appl., 196 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098850	A2	20021212	WO 2002-US17411	20020603
WO 2002098850	A3	20030424		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2448418	AA	20021212	CA 2002-2448418	20020603
EP 1397340	A2	20040317	EP 2002-734640	20020603
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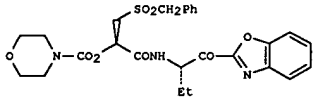
CN 1512983	A	20040714	CN 2002-811152	20020603
BR 2002010912	A	20040831	BR 2002-10912	20020603
JP 2004535422	T2	20041125	JP 2003-501840	20020603
ZA 2003008392	A	20050128	ZA 2003-8392	20031028
US 2004142999	A1	20040722	US 2003-719080	20031121
PRIORITY APPLN. INFO.:			US 2001-295301P	P 20010601
			WO 2002-US17411	W 20020603

OTHER SOURCE(S): MARPAT 138:24946
GI



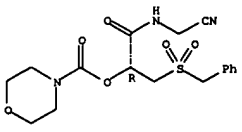
I

AB The invention relates to compds. R3C(X2)(X7)CO-X1 [X1 = NHC(R1)(R2)X3 or NHX4; X2 = H, F, OH, OR4, NHR15, or NR17R18; X7 = H or X2 = X7 = F; R3 = alkyl or CR62X6; X3 = cyano, CR7R8R16, CR6(OR6)2, CH2COR16, CH:CHSO2R5, COCF2CONR52, COCONR5R6, COCO2R5, COCH2OR5, COCH2NR6SO2R5, or COCOR5; where R5 is H or (un)substituted alkyl; R6 is H, OH or NR5R6 is a ring; R7 is H, alkyl and R8 is OH or CR7R8 are oxo; R16 is H, X4, CF3, NR6OR6, etc.; X4 comprises a heteromono- or -bicyclic ring; R1 = H, alkyl; R2 = H, cyano; R2 = H, cyano, -X5-NR122, -X5-NR12COR12, etc., where X5 is a bond or alkylene and R12 is H, alkyl, or haloalkyl; or CR1R2 may form a ring; R4 = alkylene-NR122, alkylene-NR12-COR12, etc.; X6 = -X5-NR122, -X5-NR12COR12, etc.; R15 = H, alkyl; R17, R18 = (un)substituted alkyl (with provisos)] and their pharmaceutically acceptable salts and N-oxides as selective cathepsin S inhibitors for use as therapeutic agents. Thus, ester I was prepd. via amide coupling reaction and showed Ki .ltorsim. 0.01 μM for inhibition of cathepsin S.

IT **477938-46-8P 477938-51-5P 477938-54-8P**
477938-55-9P 477938-65-1P 477938-71-9P
477938-86-6P 477938-98-0P 477938-99-1P
477939-00-7P 477939-06-3P 477939-07-4P
477939-27-8P 477939-28-9P 477939-29-0P
477939-30-3P 477939-31-4P 477939-32-5P
477939-82-5P 477939-83-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide compds. and compns. as selective cathepsin S inhibitors)

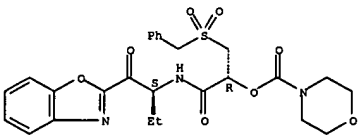
RN 477938-46-8 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



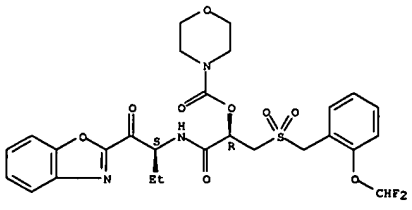
RN 477938-51-5 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[[(1S)-1-(2-benzoxazolylcarbonyl)propyl]amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



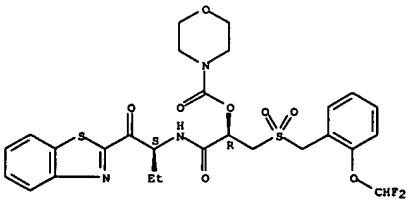
RN 477938-54-8 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[[(1S)-1-(2-benzoxazolylcarbonyl)propyl]amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



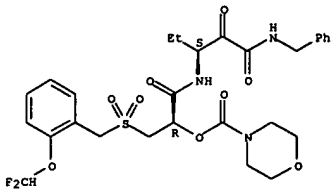
RN 477938-55-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[[(1S)-1-(2-benzothiazolylcarbonyl)propyl]amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



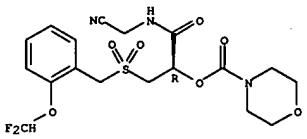
RN 477938-65-1 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-[[(1S)-1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



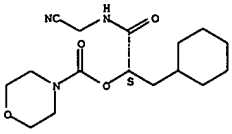
RN 477938-71-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[(cyanomethyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477938-86-6 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

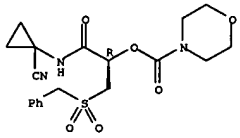
Absolute stereochemistry.



RN 477938-98-0 CAPLUS

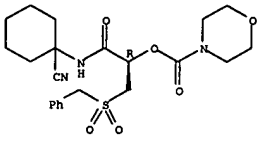
RN 477939-07-4 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[(1-cyanocyclohexyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477939-27-8 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-(2-benzoxazolylcarbonyl)propyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

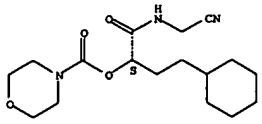


RN 477939-28-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-(cyclohexylmethyl)-2-[[(1S)-1-(oxazolo[4,5-b]pyridin-2-ylcarbonyl)propyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

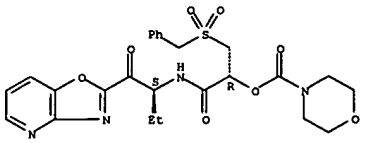
RN 477938-99-1 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-[[(cyanomethyl)amino]carbonyl]-3-cyclohexylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



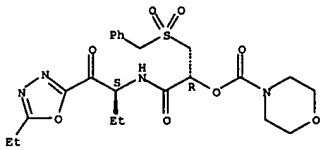
RN 477939-00-7 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[[(1S)-1-(oxazolo[4,5-b]pyridin-2-ylcarbonyl)propyl]amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



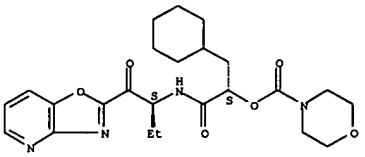
RN 477939-06-3 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[[(1S)-1-[(5-ethyl-1,3,4-oxadiazol-2-yl)carbonyl]propyl]amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



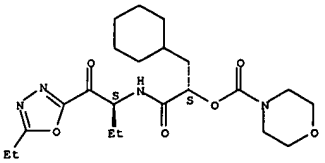
RN 477939-08-5 CAPLUS
CN 4-Morpholinecarboxylic acid, (1R)-2-[(1-cyanocyclopropyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



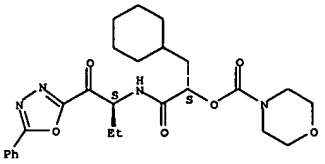
RN 477939-29-0 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-(cyclohexylmethyl)-2-[[(1S)-1-[(5-ethyl-1,3,4-oxadiazol-2-yl)carbonyl]propyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



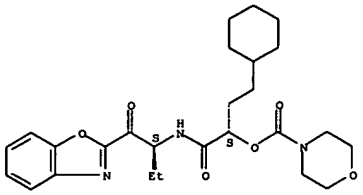
RN 477939-30-3 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-(cyclohexylmethyl)-2-oxo-2-[[(1S)-1-[(5-phenyl-1,3,4-oxadiazol-2-yl)carbonyl]propyl]amino]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

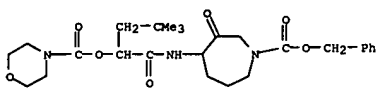


RN 477939-31-4 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-1-[[[(1S)-1-(2-benzoxazolylcarbonyl)propyl]amino]carbonyl]-3-cyclohexylpropyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

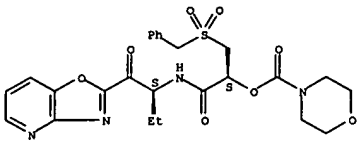


RN 477939-32-5 CAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[4,4-dimethyl-2-[(4-morpholinylcarbonyl)oxy]-1-oxopentyl]amino]hexahydro-3-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)



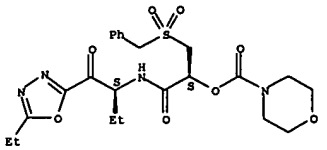
RN 477939-82-5 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-(oxazolo[4,5-b]pyridin-2-ylcarbonyl)propyl]amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477939-83-6 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[(5-ethyl-1,3,4-oxadiazol-2-yl)carbonyl]propyl]amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl ester (9CI) (CA INDEX NAME)

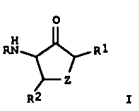
Absolute stereochemistry.



ACCESSION NUMBER: 2002:555477 CAPLUS
DOCUMENT NUMBER: 137:125390
TITLE: Preparation of amino acid-derived 3-oxotetrahydrofurans or -thiophenes and 3-oxocyclopentanes as inhibitors of cruzipain and other cysteine proteases
INVENTOR(S): Quibell, Martin
PATENT ASSIGNEE(S): Incenta Limited, UK
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057248	A2	20020725	WO 2002-GB188	20020117
WO 2002057248	A3	20021003		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1358174	A2	20031105	EP 2002-732146	20020117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004522737	T2	20040729	JP 2002-557929	20020117
US 2004127424	A1	20040701	US 2004-466355	20040108
PRIORITY APPLN. INFO.:			GB 2001-1177 A	20010117
			US 2001-275360P P	20010313
			WO 2002-GB188 W	20020117

OTHER SOURCE(S): MARPAT 137:125390
GI

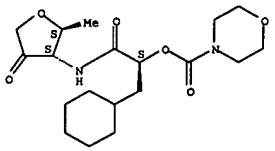


I

AB Title compds. I [R1 = H, alkyl, cycloalkyl, aryl, arylalkyl; Z = O, S, CH2; R2 = alkyl, cycloalkyl, aryl, arylalkyl; R = U-Vm-Wn-Xm'-Y, where Y =
CHR3CO, CR3R4CO (R3, R4 = any group given for R1) or R3 and R4 may form a

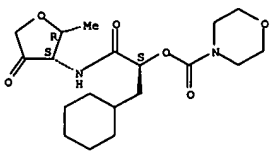
3- to 6-membered ring; X = CR9R10 (R9-R13 = any group given for R1); W = O, S, CO, SO, SO2, NR11; V = CO, CS, SO, SO2, SO2NH, O2C, NHCO, NHSO, NHSO2, O2CNH, CONH, or CR12R13; m, m' = 0-3, n = 0 or 1; U = a stable 5- to 7-membered monocyclic or 8- to 11-membered bicyclic ring contg. 0-4 heteroatoms (provided that for m > 1, Vm contains a max. of one carbonyl or sulfonyl group)] were prepd. as inhibitors cruzipain (a gene product of
Trypanosoma cruzi parasite) and other cysteine proteases for use as therapeutic agents, for example in the treatment of Chagas' disease. Thus, (2R,3S)-4-methyl-2-[2-oxo-2-(3-phenylpyrrol-1-yl)ethyl]pentanoic acid (2-methyl-4-oxotetrahydrofuran-3-yl)amide was prepd. by amidation reaction and assayed for inhibition of cruzipain, bovine cathepsin S, and human cathepsins L and K (Ki = <5, >50, >100, and >5 μM, resp.).
IT **443918-37-4P 443918-48-7P 443918-62-5P**
443918-74-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid-derived oxotetrahydrofurans or -thiophenes and
oxocyclopentanes as inhibitors of cruzipain and other cysteine proteases)
RN 443918-37-4 CAPLUS
CN L-erythro-2-Pentulose, 1,4-anhydro-3-[[(2S)-3-cyclohexyl-2-[(4-morpholinylcarbonyl)oxy]-1-oxopropyl]amino]-3,5-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



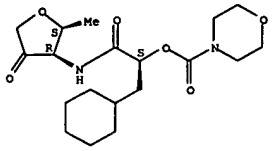
RN 443918-48-7 CAPLUS
CN D-threo-2-Pentulose, 1,4-anhydro-3-[[(2S)-3-cyclohexyl-2-[(4-morpholinylcarbonyl)oxy]-1-oxopropyl]amino]-3,5-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



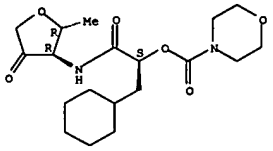
L6 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 443918-62-5 CAPLUS
CN L-threo-2-Pentulose, 1,4-anhydro-3-[[(2S)-3-cyclohexyl-2-[(4-morpholinylcarbonyl)oxy]-1-oxopropyl]amino]-3,5-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 443918-74-9 CAPLUS
CN D-erythro-2-Pentulose, 1,4-anhydro-3-[[(2S)-3-cyclohexyl-2-[(4-morpholinylcarbonyl)oxy]-1-oxopropyl]amino]-3,5-dideoxy- (9CI) (CA INDEX NAME)

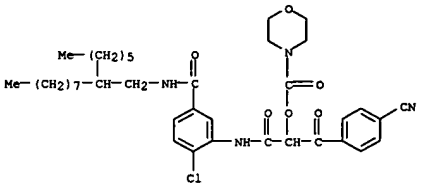
Absolute stereochemistry.



L6 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:106181 CAPLUS
DOCUMENT NUMBER: 128:210809
TITLE: Silver halide color photographic material containing a DIR coupler and a hydrazine derivative
INVENTOR(S): Nakagawa, Hajime; Nakamine, Isamu
PATENT ASSIGNEE(S): Fuji Photo Film Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 118 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10039464	A2	19980213	JP 1996-209373	19960722
PRIORITY APPLN. INFO.:			JP 1996-209373	19960722

AB Claimed color photog. material is characterized by (1) that at least one emulsion layer contains, in the amount of ≥50% of total grain-projected area, tabular grains with AgCl content of ≥60 mol% and aspect ratio of ≤2.0 and (2) that at least one emulsion layer contains a compound; AOC(:O)NX1CX2X3DI, (A = coupler moiety; X1 = heterocyclic group, CX3X5Y; Y = SO2R1, SO2NR1R2, CO2Z1, CN, CF2, CCl2; R1, R2 = H, alkyl, cycloalkyl, alkenyl, aryl, heterocyclic group; Z = H, cycloalkyl, alkenyl, aryl, heterocyclic group; X2, X3, X4, X5 = H, substituent; DI = development-inhibiting moiety), a hydrazide R11NHNHXR12, (R11 = aryl, heterocyclic group; R12, R13 = H, alkyl, alkenyl, aryl, heterocyclic group; X = XO2CO, COCO, CO2, CONR13, COCO2, COCONR13) and a dye-forming coupler. It has an improved sharpness and color reproduction quality, and suitably used as a multilayer color neg. film.
IT 204057-08-9
RL: DEV (Device component use); USES (Uses)
(coupler; color photog. material containing DIR compound and hydrazine derivative
to improve sharpness and color reproduction quality)
RN 204057-08-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[2-chloro-5-[[(2-hexyldecyl)amino]carbonyl]phenyl]amino]carbonyl]-2-(4-cyanophenyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

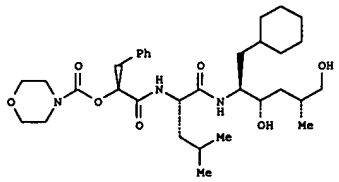


L6 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

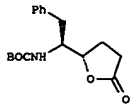
L6 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:978676 CAPLUS
DOCUMENT NUMBER: 124:30427
TITLE: Preparation of antimalarial aspartic protease inhibitors.
INVENTOR(S): Russell, Mark A.; Mueller, Richard A.; Bryant, Martin L.; Hanson, Gunnar H.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9519958	A1	19950727	WO 1995-US17	19950112
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2181551	AA	19950727	CA 1995-2181551	19950112
AU 9515968	A1	19950808	AU 1995-15968	19950112
EP 741696	A1	19961113	EP 1995-907965	19950112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1139427	A	19970101	CN 1995-191359	19950112
JP 09508365	T2	19970826	JP 1995-519566	19950112
PRIORITY APPLN. INFO.:			US 1994-186379	A1 19940125
			WO 1995-US17	W 19950112

OTHER SOURCE(S): MARPAT 124:30427
GI



I



II

AB AR6NCHR1CHOP1CHR2CHR5CR3R4OP2 (P1, P2 = H, alkanoyl; P1P2 = CO, CR7R8; R7,
R8 = H, alkyl, aryl, cycloalkyl, cycloalkylalkyl, aralkyl; R1-R4 = alkyl, aryl, cycloalkyl, cycloalkylalkyl, alkenylalkyl, alkynylalkyl, aralkyl; R5
= Me, Et, Pr, Bu, Me2CHCH2, Me3C, aryl, cycloalkyl, aralkyl, etc.; R6 = H,
alkyl; A = alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, R11R12NCHR10C:Y; Y = O, S; R10 = H, CH2SO2NH2, cyanoalkyl, aralkyl, heteroaryl, alkenyl, alkynyl, etc.; R11 = H, alkoxycarbonyl, aralkoxycarbonyl, alkanoyl, aroyl, heteroaralkoxycarbonyl,
alkyl, aryl, hydroxyalkyl, etc.; R12 = H, alkyl, aralkoxycarbonylalkyl, aminocarbonylalkyl, etc.), were prepared Thus, title compound (I), prepared by
solution phase methods from lactone (II), at 10 μM gave 45% inhibition of
Plasmodium falciparum HB3 late ring stage cultures.

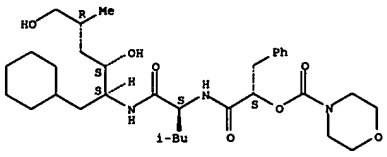
IT **171347-68-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antimalarial aspartic protease inhibitors)

RN 171347-68-5 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[1-[[[1-(cyclohexylmethyl)-2,5-dihydroxy-4-methylpentyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2R*,4S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



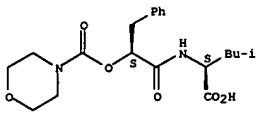
IT **122994-25-6**

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antimalarial aspartic protease inhibitors)

RN 122994-25-6 CAPLUS

CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-carboxy-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1995:292677 CAPLUS
DOCUMENT NUMBER: 122:122442

TITLE: Renin inhibitor: relationship between molecular structure and oral absorption

AUTHOR(S): Hashimoto, Naofumi; Fujioka, Toshihiro; Hayashi, Kunio; Odaguchi, Kunihiro; Toyoda, Tatsuo; Nakamura, Masuhisa; Hirano, Koichiro

CORPORATE SOURCE: Shionogi Research Lab., Shionogi & Co., Ltd., Osaka, 553, Japan

SOURCE: Pharmaceutical Research (1994), 11(10), 1443-7
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

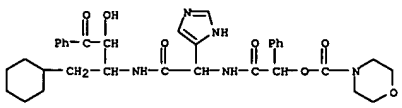
AB Common problems in developing renin inhibitors are low solubility insufficient
oral absorption, and fast hepatic clearance. We focused on the mol. structure of renin inhibitors to overcome these problems. Cyclodextrins (CD) improved the low solubility of renin inhibitors, with β-CD showing the best ability to dissolve renin inhibitors. The intestinal absorption of renin inhibitors varied with both their solubility and mol. structure. Coadministration of β-CD improved the intestinal absorption of some renin inhibitors with low solubility as measured by transport into the mesenteric vein in the absorption experiment using the rat intestinal loop.
Substitutions at both the N and C terminals was essential for absorption from the small intestine. A naphthyl group at the N-terminal further improved intestinal absorption. A carrier system appeared to be involved in the intestinal absorption of some renin inhibitors. N-methylation at the amide bond of thiazolylalanine suppressed the high hepatic clearance of one of the test compds. which was well adsorbed from the small intestine and it improved its oral bioavailability.

IT **160889-90-7 160889-91-8 160889-95-2**

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(renin inhibitor: relationship between mol. structure and oral absorption)

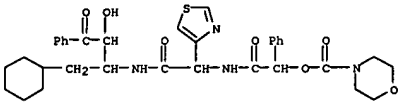
RN 160889-90-7 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-3-oxo-3-phenylpropyl]amino]-1-(1H-imidazol-4-yl)-2-oxoethyl]amino]-2-oxo-1-phenylethyl ester (9CI) (CA INDEX NAME)



RN 160889-91-8 CAPLUS

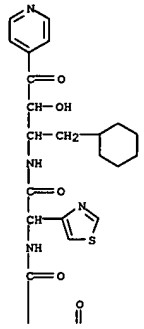
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-3-oxo-3-phenylpropyl]amino]-2-oxo-1-(4-thiazolyl)ethyl]amino]-2-oxo-1-phenylethyl ester (9CI) (CA INDEX NAME)



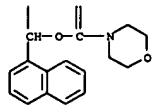
RN 160889-95-2 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-3-oxo-3-[4-pyridinyl)propyl]amino]-2-oxo-1-(4-thiazolyl)ethyl]amino]-1-(1-naphthalenyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L6 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

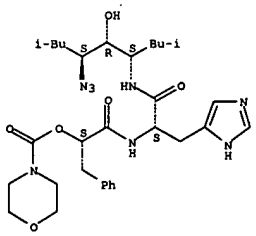
ACCESSION NUMBER: 1995:67122 CAPLUS
DOCUMENT NUMBER: 122:230104
TITLE: Potent renin inhibition activity of tetrapeptide mimetics with a 1,2-hydroxyazidoethylene group connecting the P1 and P1' residues
AUTHOR(S): Almquist, R. G.; Nakazato, A.; Kameo, K.; Fukushima, H.; Chao, W.-R.
CORPORATE SOURCE: Biogen Inc., Cambridge, MA, 02142, USA
SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 13th (1994), Meeting Date 1993, 281-3. Editor(s): Hodges, Robert S.; Smith, John A. ESCOM: Leiden, Neth.
CODEN: 60LXAW
DOCUMENT TYPE: Conference
LANGUAGE: English

AB When tested with human renin, tetrapeptide mimetics with a 1,2-hydroxyazidoethylene group were more potent than compds. with a hydroxyamino group. Also the stereochem. for the most active isomer in the hydroazido series was the same as that reported earlier for the most active isomer in the dihydroxy series.

IT **148945-39-5 162128-97-4 162128-98-5 162128-99-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(potent human renin inhibition activity of tetrapeptide mimetics with a 1,2-hydroxyazidoethylene group connecting the P1 and P1' residues)

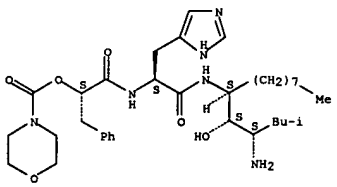
RN 148945-39-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[3-azido-2-hydroxy-5-methyl-1-(2-methylpropyl)hexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



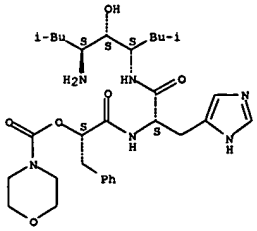
RN 162128-97-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[3-amino-2-hydroxy-5-methyl-1-(2-methylpropyl)hexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2R*,3R*]]- (9CI) (CA INDEX NAME)

L6 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



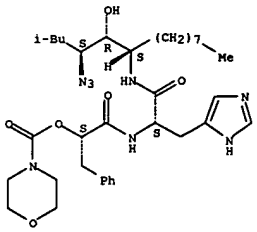
L6 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



RN 162128-98-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(2-azido-1-hydroxy-4-methylpentyl)nonyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1R-[1R*[S*[S*(S*)]],2S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 162128-99-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(2-amino-1-hydroxy-4-methylpentyl)nonyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*[R*(R*)]],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:207844 CAPLUS
DOCUMENT NUMBER: 120:207844
TITLE: Role of intestinal transport and first pass liver extraction on oral delivery of renin inhibitor compounds
AUTHOR(S): Kararli, Tugrul T.; Farhadieh, Bahram; Bittner, Steve; Babler, Maribeth; Yang, Po Chang; Walsh, Gerald M.
CORPORATE SOURCE: G.D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: International Journal of Pharmaceutics (1994), 102(1-3), 177-84
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English

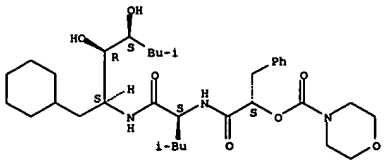
AB The absolute bioavailabilities of three renin inhibitor compds., one uncharged (compound I) and two pos. charged (compds. II and III), were found to be comparable (1-3%). To determine the role of intestinal transport and first pass liver extraction (FPLE) in the oral delivery of these compds. i.v., intraportal, intraduodenal and i.p. studies were performed in the rat. In the intraduodenal studies, drug solns. were injected into the duodenum of anesthetized rats and portal and systemic blood was collected. In the intraportal studies, the drug solns. were injected into the portal vein and systemic blood was collected. From the ratio of the area under the drug concentration-time curves (tAUC) for the oral and intraportal studies, the extent of intestinal transport of compds. I-III was estimated as 9.7, 2.2 and 2.2%, resp. In the intraduodenal studies the maximum portal plasma concns. of compds. I-III were 2.8, 0.5 and 0.2 μg/mL, resp. The tAUC of compound I in portal plasma was 8-26-times higher than those for compds. II and III. From comparison of the intraportal and i.v. tAUC values, the FPLE of compds. I-III was estimated as 76 ± 4, 61 ± 3 and 8 ± 23% (mean ± SE), resp. Overall, the results indicated that the intestinal transport and FPLE of compound I was the highest among the three analogs. Compound II showed low intestinal transport and high FPLE and compound III showed low intestinal transport and low but variable FPLE.

IT **120729-15-9**
RL: BIOL (Biological study)
(intestinal transport and liver extraction of, oral bioavailability in relation to)

RN 120729-15-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

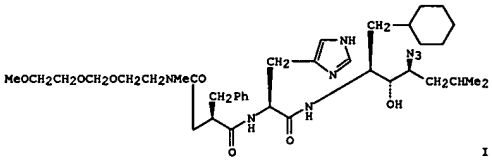


L6 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:496179 CAPLUS
DOCUMENT NUMBER: 119:96179
TITLE: Hydroxy azido derivatives and related compounds as renin inhibitors
INVENTOR(S): Almquist, Ronald G.; Nakazato, Atsuro
PATENT ASSIGNEE(S): SRI International, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9221696	A1	19921210	WO 1992-US3893	19920506
W: CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5268361	A	19931207	US 1991-712311	19910607
CA 2110381	AA	19921210	CA 1992-2110381	19920506
EP 587767	A1	19940323	EP 1992-913519	19920506
R: DE, FR, GB, IT, NL				
JP 06508137	T2	19940914	JP 1992-500421	19920506
PRIORITY APPLN. INFO.:			US 1991-712311	A 19910607
			WO 1992-US3893	W 19920506

OTHER SOURCE(S): MARPAT 119:96179
GI



I

AB RCONR1CHR2CONHCHR3CH(OH)CR4R5N3 [R = CHR6CH2R7, CR6:CHR7; R1 = H, alkyl; R2 = alkyl, alkenyl, alkoxyalkyl, alkoxy, CH2Ph, heterocyclylmethyl; R3 = alkyl, cycloalkylmethyl, CH2Ph; R4 = H, alkyl, vinyl, aralkyl; R5 = H, alkyl; R6 = H, (un)substituted alkyl; R7 = alkyl, cycloalkyl, (un)substituted aryl] were prepared Thus, the histidine derivative I was obtained from Me3CO2C-Ph-OMe, protected histidine, and (R)-MeOCH2CH2OCH2OCH2CH2NMeCOCH2CH(CH2Ph)CO2H in 7 steps. I had a renin-inhibiting ED50 of 0.008 nM.

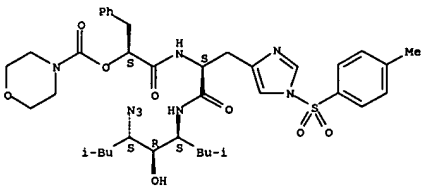
IT **148945-38-4P 148975-73-9P 148975-79-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and detosylation of)

RN 148945-38-4 CAPLUS

L6 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CN 4-Morpholinecarboxylic acid, 2-[[2-[[3-azido-2-hydroxy-5-methyl-1-(2-methylpropyl)hexyl]amino]-1-[[1-[(4-methylphenyl)sulfonyl]-1H-imidazol-4-yl]methyl]-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

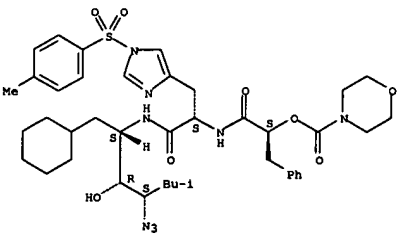
Absolute stereochemistry.



RN 148975-73-9 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[3-azido-1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]amino]-1-[[1-[(4-methylphenyl)sulfonyl]-1H-imidazol-4-yl]methyl]-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

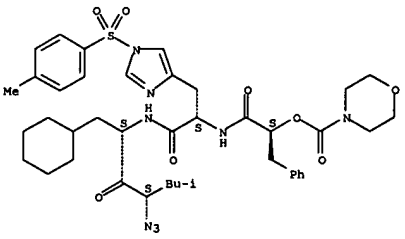


RN 148975-79-5 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[3-azido-1-(cyclohexylmethyl)-5-methyl-2-oxohexyl]amino]-1-[[1-[(4-methylphenyl)sulfonyl]-1H-imidazol-4-yl]methyl]-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

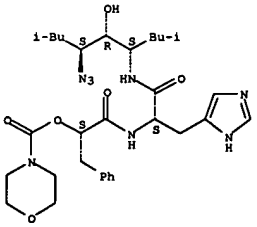


IT **148945-39-5P 148975-74-0P 148975-80-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and renin-inhibiting activity of)

RN 148945-39-5 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[3-azido-2-hydroxy-5-methyl-1-(2-methylpropyl)hexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

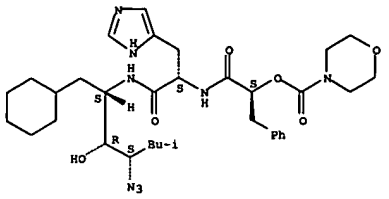


RN 148975-74-0 CAPLUS

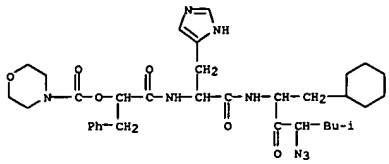
CN 4-Morpholinecarboxylic acid, 2-[[2-[[3-azido-1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 148975-80-8 CAPLUS
CN 4-Morpholinecarboxylic acid,
2-[[2-[[3-azido-1-(cyclohexylmethyl)-5-methyl-2-oxohexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

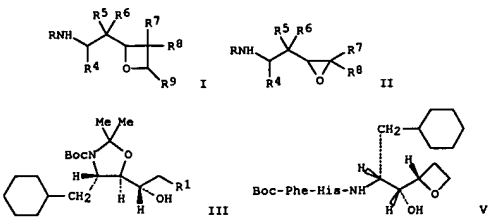


L6 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:409168 CAPLUS
DOCUMENT NUMBER: 119:9168
TITLE: Preparation of oxiranyl and oxetanyl renin inhibiting compounds
INVENTOR(S): Rosenberg, Saul H.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9222313	A1	19921223	WO 1992-US4423	19920526
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5258362	A	19931102	US 1992-880250	19920513
AU 9221593	A1	19930112	AU 1992-21593	19920526
PRIORITY APPLN. INFO.:			US 1991-713475 A	19910611
			US 1992-880250 A	19920513
			WO 1992-US4423 A	19920526

OTHER SOURCE(S): MARPAT 119:9168
GI



AB The title compds. I and II [R = mimic of Phe-His dipeptide; R4 = lower alkyl, cycloalkyl, arylalkyl; R5 = H, lower alkyl, hydroxyalkyl, lower alkenyl, CHO; R6 = OH, NH2; R7 = H, lower alkyl; R8 = H, lower alkyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkyl, thioalkoxyalkyl, haloalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, cycloalkyl, cycloalkylalkyl, lower alkenyl, alkynyl, aryl, arylalkyl, heterocyclic, heterocycloalkyl; R7R8 = (CH2)n, n = 3-6; R9 = lower alkyl] or a pharmaceutically acceptable salt, ester, or prodrug of, were prepared as renin inhibitors. Thus, Reformatskii reaction of (4S,5R)-3-tert-

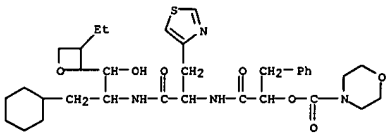
butoxycarbonyl-4-cyclohexylmethyl-2,2-dimethyloxazolidine-5-carboxaldehyde

L6 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

with benzyl bromoacetate gave hydroxy ester III (Boc = Me3CO2C; R1 = CO2CH2Ph), which was reduced with NaBH4-CaCl2 to diol III (R1 = CH2OH)
and
selectively tosylated to tosylate III (R1 = CH2O3SC6H4Me-4) (IV). Cyclization of tosylate IV to the corresponding oxetane, followed by acidic deprotection, coupling with Boc-Phe-His(Boc)-OH, and selective deblocking gave oxetanyl peptide V. Compds. I and II are useful in treating hypertension, congestive heart failure, glaucoma, and inhibiting HIV-1 and HIV-2 proteases.

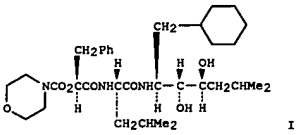
IT 147895-99-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)

RN 147895-99-6 CAPLUS
CN L-Altritol,
4,6-anhydro-1-cyclohexyl-1,2,5-trideoxy-5-ethyl-2-[[2-[[2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]amino]-1-oxo-3-(4-thiazolyl)propyl]amino]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)



L6 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:619884 CAPLUS
DOCUMENT NUMBER: 117:219884
TITLE: Enhancement of nasal delivery of a renin inhibitor in the rat using emulsion formulations
AUTHOR(S): Kararli, Tugrul T.; Needham, Thomas E.; Schoenhard, Grant; Baron, David A.; Schmidt, R. Eric; Katz, Barbara; Belonio, Bayani
CORPORATE SOURCE: G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Pharmaceutical Research (1992), 9(8), 1024-8
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



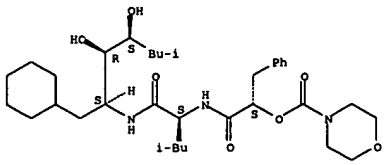
AB Nasal absorption of a renin inhibitor (I) was evaluated in two rat nasal models, one involving surgery and the other requiring no surgical intervention. Oleic acid/monoolein emulsion formulations were tested along with a control PEG 400 solution The percent absolute bioavailability of
the compound was enhanced from 3-6% (PEG 400 solution) to 15-27% when the emulsion formulations were used. The different nasal model techniques (with and without surgery) did not produce any statistical difference in the absolute bioavailability values for I. Emulsion formulations did not produce appreciable damage as assessed morphol. It is suggested the emulsion formulations containing membrane adjuvants such as oleic acid
and
monoolein can be used to enhance the nasal delivery of low-bioavailable, lipid-soluble drugs.

IT 120729-15-9
RL: BIOL (Biological study)
(nasal bioavailability of, from emulsion, membrane adjuvants enhancement of)

RN 120729-15-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

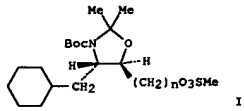
Absolute stereochemistry.

L6 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

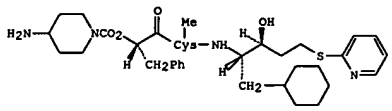


L6 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:572067 CAPLUS
DOCUMENT NUMBER: 117:172067
TITLE: Renin inhibitors containing new P1-P1' dipeptide mimetics with heterocycles in P1'
AUTHOR(S): Raddatz, Peter; Jonczyk, Alfred; Minck, Klaus Otto; Rippmann, Friedrich; Schittenhelm, Christine; Schmitges, Claus Jochen
CORPORATE SOURCE: Preclin. Pharm. Res., E. Merck Darmstadt, Darmstadt, D-6100, Germany
SOURCE: Journal of Medicinal Chemistry (1992), 35(19), 3525-36
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB A series of renin inhibitors containing new P1-P1' dipeptide mimetics are presented. The P1-P1' mimetics were obtained from 4-(cyclohexylmethyl)-5-(mesyloxyalkyl)-2,2-dimethyloxazolidines I (Boc = Me3CO2C; n = 1-3) by nucleophilic substitution of the mesylate groups with sodium salts of mercapto- and hydroxyheterocycles. Removal of the protecting groups and stepwise acylations with amino acid derivs. provided renin inhibitors with a length of a tripeptide. Replacement of P2 His by other amino acids maintained or enhanced renin inhibitory potency. By alteration of P3 Phe, compds. with IC50 values in the nanomolar range and stability against chymotrypsin were obtained. Finally, the effect of the C-terminal heterocycle on the renin inhibition was studied. Compound II was examined in vivo for its hypotensive effects. In salt-depleted cynomolgus monkeys, II inhibited plasma renin activity and lowered blood pressure after oral administration of a dose of 10 mg/kg.

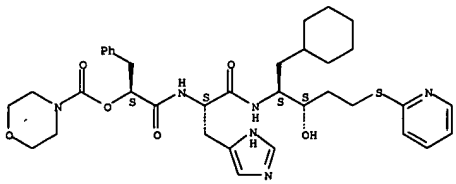
IT **143122-42-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, proteolytic stability, and renin inhibitory activity of)

RN 143122-42-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-4-(2-

L6 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

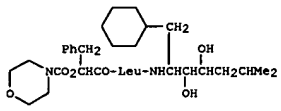
pyridinylthio)butyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:518346 CAPLUS
DOCUMENT NUMBER: 117:118346
TITLE: Oral delivery of a renin inhibitor compound using emulsion formulations
AUTHOR(S): Kararli, Tugrul T.; Needham, Thomas E.; Griffin, Marty; Schoenhard, Grant; Ferro, Leonard J.; Alcorn, Lisa
CORPORATE SOURCE: G. D. Searle Res. Dev., Skokie, IL, 60077, USA
SOURCE: Pharmaceutical Research (1992), 9(7), 888-93
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

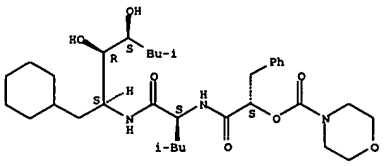
AB The oral delivery of a new renin inhibitor (I), was studied in the in vivo rat model using emulsion formulations. The components of the emulsion formulations were chosen based on their proposed effects on membrane structure, membrane fluidity, and solute transport. The percent absolute bioavailability (%AB) of I was increased from 0.3% (water suspension) to 5.1% when long-chain unsatd. fatty acid (oleic acid, linoleic acid, etc.)- and mono- and diglyceride (monoolein, dilaurin, etc.)-containing emulsion formulations were used. Considering very high first-pass liver extraction of the compound (80%), it is suggested that emulsion formulations increased the intestinal transport of the compound significantly. The solubility of I in aqueous media with and without bile salt (20mM) was found to be low (.apprx.1 μg/mL). Incubation in 0.01N HCl did not affect the particle size of the emulsion. The titration of oleic acid/monoolein emulsion in a pH 6.5 medium with a mixed bile salt system indicated reduction in the particle size of the emulsion. Drug precipitation was observed above 30mM bile salt concns. No drug crystals could be detected in the intestinal contents of the rats when emulsion formulations were ingested. These results suggest that in the intestine of the animals, the particle size of the emulsions is reduced in the presence of bile fluid while the drug resides primarily in the oil phase. The mechanism of enhanced transport of I from the emulsion formulations is discussed along with the possibility of cotransport from the drug and oil. Emulsion formulations can be a potential delivery form for low-bioavailable lipid-soluble drugs.

IT **120729-15-9**
RL: BIOL (Biological study)
(oral delivery of, as renin inhibitor, emulsion for)

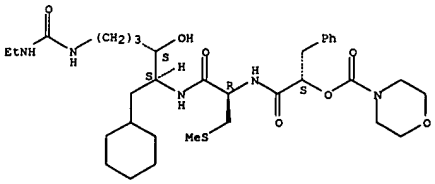
RN 120729-15-9 CAPLUS

L6 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L6 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:490797 CAPLUS
DOCUMENT NUMBER: 117:90797
TITLE: Preparation of peptides containing glycolic acid derivatives as renin inhibitors
INVENTOR(S): Raddatz, Peter Dr; Schmitges, Claus J.; Minck, Klaus Otto
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 446751	A1	19910918	EP 1991-103213	19910304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4008403	A1	19910919	DE 1990-4008403	19900316
CA 2038282	AA	19910917	CA 1991-2038282	19910314
AU 9172906	A1	19910919	AU 1991-72906	19910314
AU 650442	B2	19940623		
HU 59939	A2	19920728	HU 1991-846	19910314
HU 207508	B	19930428		
ZA 9101951	A	19911224	ZA 1991-1951	19910315
JP 05032609	A2	19930209	JP 1991-154154	19910315
US 5147857	A	19920915	US 1991-670677	19910318
PRIORITY APPLN. INFO.:			DE 1990-4008403 A	19900316

OTHER SOURCE(S): MARPAT 117:90797
AB X-O-CR1R2-CO-Y-NR3-CHR4-C(:R5)-CH2CR6R7-Z [I; X = H, aryl, aralkyl, heterocyclyl, acyl, etc.; Y = 0 or 1 amino acid residue, e.g., Ala, β-Ala, Arg; Z = cyano, (substituted) aminomethyl, (substituted) ureidomethyl, etc.; R1, R3, R6, R7 = H, aryl, aralkyl, heterocyclyl, acyl, etc.; R2, R4 = H, aryl, aralkyl, heterocyclyl, etc.; R5 = (H, OH), (H, NH2), O] and their salts, renin inhibitors and therefore useful for treating hypertension (no data), were prepared (4S,5S)-BOC-His(BOM)-NHCHQ1CH(OH)(CH2)3NHCONHEt [BOM = benzyloxymethyl, Q1 = cyclohexylmethyl] was deprotected and condensed with QCO2Pla-H [Q = 4-(tert-butoxycarbonyl)piperidino; Pla = OCH(CH2Ph)CO] (preparation given) to give (4S,5S)-QCO2Pla-His(BOM)-NHCHQ1CH(OH)(CH2)3NHCONHEt, which was hydrogenolyzed over Pd/C in EtOH to give (4S,5S)-QCO2Pla-His-NHCHQ1CH(OH)(CH2)3NHCONHEt. Pharmaceutical tablets, capsules, etc., containing I were formulated.
IT **138893-89-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)
RN 138893-89-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 7-(cyclohexylmethyl)-8-hydroxy-4-[(methylthio)methyl]-2,5,13-trioxo-1-(phenylmethyl)-3,6,12,14-tetraazahexadec-1-yl ester, [1S-(1R*,4S*,7R*,8R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

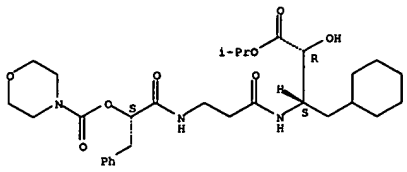
L6 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:449268 CAPLUS
DOCUMENT NUMBER: 117:49268
TITLE: Preparation of peptides for treatment of renin-dependent hypertension and aldosteronism.
INVENTOR(S): Raddatz, Peter; Sombroek, Johannes; Schmitges, Claus J.; Minck, Klaus Otto
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4027457	A1	19920305	DE 1990-4027457	19900830
EP 474008	A1	19920311	EP 1991-113841	19910819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2050092	AA	19920301	CA 1991-2050092	19910828
ZA 9106861	A	19920527	ZA 1991-6861	19910829
JP 04297447	A2	19921021	JP 1991-298603	19910830
AU 9183527	A1	19930408	AU 1991-83527	19910830
HU 62603	A2	19930528	HU 1991-2826	19910830
PRIORITY APPLN. INFO.:			DE 1990-4027457 A	19900830

OTHER SOURCE(S): MARPAT 117:49268
AB X-W-CR1R2-CO-Y-NH-CHR3-CR4-CO2R5 [I; X = H, acyl; W = O, NH; R1 = H, A; R2, R3 = H, A, (substituted) Ph, naphthyl; R4 = (H, OH), (H, NH2), O; R5 = H, A, cycloalkyl; Y = β-Ala, isoserine residue], useful for treating renin-dependent hypertension and aldosteronism (no data), were prepared Me 3S-amino-4-cyclohexyl-2R-hydroxybutyrate was condensed with 4-BOC-aminopiperidinocarbonylphenylalanyl-β-alanine in CH2Cl2 containing N-methylmorpholine, HOBt, and DCC at 0-5° for 12 h to give Me 3S-(4-BOC-amino-piperidinocarboylphenylalanyl-β-alanylamino)-4-cyclohexyl-2R-hydroxybutyrate. Tablets, capsules, injections, etc., containing I were formulated.
IT **141770-80-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for treatment of hypertension and hyperaldosteronism)
RN 141770-80-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[3-[[1-(cyclohexylmethyl)-2-hydroxy-3-(1-methylethoxy)-3-oxopropyl]amino]-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*(R*),2S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

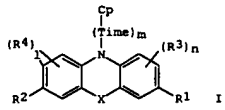


L6 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:245210 CAPLUS
DOCUMENT NUMBER: 116:245210
TITLE: Silver halide color photographic material
INVENTOR(S): Ikesu, Satoru
PATENT ASSIGNEE(S): Konica Co., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04037746	A2	19920207	JP 1990-143897	19900601
PRIORITY APPLN. INFO.:			JP 1990-143897	19900601

GI

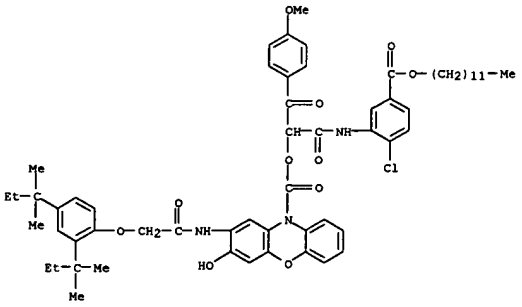


AB The title material contains a coupler represented by general structure I (Cp = a coupler residue; Time = a timing group; X = O, S, etc.; R1 to R4 = H or a substituent; n, l = an integer; n, l ≥1; m = 0 or 1). The title material gives excellent color reproduction

IT **141549-44-2**
RL: TEM (Technical or engineered material use); USES (Uses)
(photog. coupler)

RN 141549-44-2 CAPLUS
CN 10H-Phenoxazine-10-carboxylic acid, 2-[[[2,4-bis(1,1-dimethylpropyl)phenoxy]acetyl]amino]-3-hydroxy-, 1-[[[2-chloro-5-[(dodecyloxy)carbonyl]phenyl]amino]carbonyl]-2-(4-methoxyphenyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

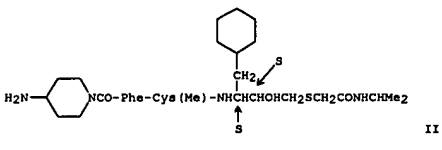


L6 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:152416 CAPLUS
DOCUMENT NUMBER: 116:152416
TITLE: Preparation of dipeptide derivatives as renin inhibitors
INVENTOR(S): Raddatz, Peter; Minck, Klaus Otto; Schmitges, Claus J.
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 464517	A2	19920108	EP 1991-110259	19910621
EP 464517	A3	19930407		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4021512	A1	19920116	DE 1990-4021512	19900705
CA 2046112	AA	19920106	CA 1991-2046112	19910703
AU 9180217	A1	19920109	AU 1991-80217	19910704
ZA 9105243	A	19920429	ZA 1991-5243	19910705
JP 04305562	A2	19921028	JP 1991-259947	19910705
HU 61321	A2	19921228	HU 1991-2282	19910705
PRIORITY APPLN. INFO.:			DE 1990-4021512 A	19900705

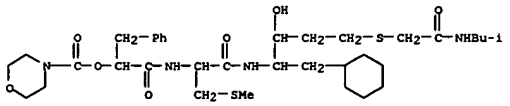
OTHER SOURCE(S): MARPAT 116:152416
GI



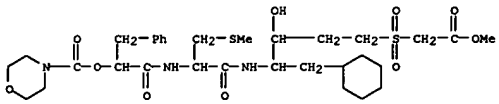
AB Title compds. XWCR1R2COYNHCHR4CR5CH2(CR6R7)rS(O)tCH2COVR3 [I; X = R8, R8OCmH2mCO, R8CmH2mO2C, etc.; W = O, NH, CH2, S; Y = O, Ala, Arg, Asn, etc.; V = O, NH; R1, R6, R7 = H, C1-8 alkyl; R2-R4, R8 = H, C1-8 alkyl, (substituted) Ph, (substituted) naphthyl, (substituted) 5- or 6-membered heterocyclyl, etc.; R5 = (H, OH), (H, NH2), O; m = 0-10; r = 0-3; t = 0-2] were prepared as renin inhibitors (no data). Thus, II was prepared by standard coupling methods. Formulations of I were prepared

IT **139624-61-6P 139624-79-6P 139625-25-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)

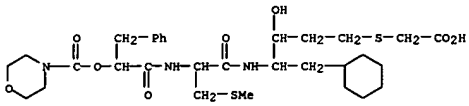
L6 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 139624-61-6 CAPLUS
CN L-threo-Pentitol, 1-cyclohexyl-1,2,4-trideoxy-5-S-[2-[(2-methylpropyl)amino]-2-oxoethyl]-2-[[3-(methylthio)-2-[[2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]amino]-1-oxopropyl]amino]-5-thio-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)



RN 139624-79-6 CAPLUS
CN L-threo-Pentitol, 1-cyclohexyl-1,2,4,5-tetradeoxy-5-[(2-methoxy-2-oxoethyl)sulfonyl]-2-[[3-(methylthio)-2-[[2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]amino]-1-oxopropyl]amino]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)



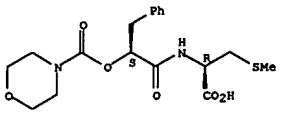
RN 139625-25-5 CAPLUS
CN L-threo-Pentitol, 5-S-(carboxymethyl)-1-cyclohexyl-1,2,4-trideoxy-2-[[3-(methylthio)-2-[[2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]amino]-1-oxopropyl]amino]-5-thio-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)



IT **139625-49-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of renin inhibitors)
RN 139625-49-3 CAPLUS
CN L-Cysteine, S-methyl-N-[2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

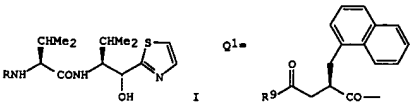
L6 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L6 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:42060 CAPLUS
DOCUMENT NUMBER: 116:42060
TITLE: Preparation of N1-(1-heteroaryl-1-hydroxyalk-2-yl)-N2-(3-alkoxycarbonyl-2-arylmethylpropionyl)-α-aminoalkanamides and analogs as renin inhibitors
INVENTOR(S): Albright, Jay Donald; Howell, Charles Frederick; Levin, Jeremy Ian; Sum, Fuk Wah; Reich, Marvin Fred
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Eur. Pat. Appl., 106 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 427939	A2	19910522	EP 1990-117977	19900919
EP 427939	A3	19911106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
CA 2027125	AA	19910412	CA 1990-2027125	19901009
JP 03178962	A2	19910802	JP 1990-272062	19901009
AU 9064505	A1	19910418	AU 1990-64505	19901010
US 5104869	A	19920414	US 1990-605067	19901025
PRIORITY APPLN. INFO.:			US 1989-419810 A	19891011

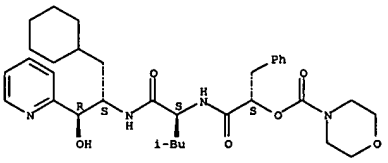
OTHER SOURCE(S): MARPAT 116:42060
GI



AB QNR3CHR4CONR5CHR6CH(OH)A [A = (un)substituted heteroaryl; Q = (R)-R1COWCHR2CO; R1 = alkoxy, NR7R8; R7 = H, alkyl; R8 = (un)substituted alkyl; or NR7R8 = heterocyclyl; R2 = (un)substituted arylmethyl; R3, R5 = H, Me; R4 = (amino)alkyl, PhCH2, alkoxy, heteroarylmethyl, etc.; R6 = (alkoxy)alkyl, PhCH2, cyclohexylmethyl, etc.; W = CH2, O] were prepared Thus, QOH (Q = acylisobutanoyl group Q1; R9 = OCMe3) (preparation given) was condensed with leucylaminopentanol I (R = H) (preparation given) to give I (R = Q1, R9 = OCMe3). I [R = Q1, R9 = 2-(N-methyl-2-pyrrolyl)ethylamino] had IC50 of 3.3 + 10-8M against angiotensin I generation in vitro.
IT **138275-97-5P 138275-98-6P 138276-01-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)
RN 138275-97-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-[[[1-(cyclohexylmethyl)-2-hydroxy-2-(2-pyridinyl)ethyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*]]- (9CI) (CA INDEX NAME)

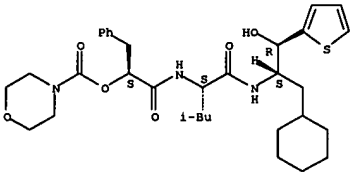
Absolute stereochemistry.

L6 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 138275-98-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-[[[1-(cyclohexylmethyl)-2-hydroxy-2-(2-thienyl)ethyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*]]- (9CI) (CA INDEX NAME)

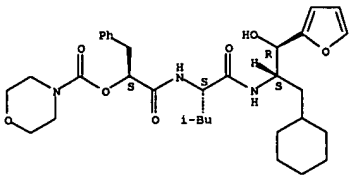
Absolute stereochemistry.



RN 138276-01-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-[[[1-(cyclohexylmethyl)-2-(2-furanyl)-2-hydroxyethyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

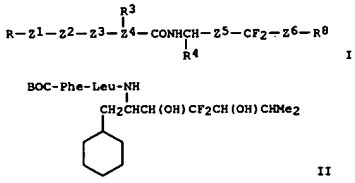


L6 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:536788 CAPLUS
DOCUMENT NUMBER: 115:136788
TITLE: Preparation of renin-inhibiting difluorodiol-containing peptides
INVENTOR(S): Sham, Hing L.; Rosenberg, Saul H.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Eur. Pat. Appl., 68 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 416393	A1	19910313	EP 1990-116225	19900824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 9061934	A1	19910314	AU 1990-61934	19900828
CA 2024698	AA	19910306	CA 1990-2024698	19900905
JP 03148246	A2	19910625	JP 1990-235483	19900905
PRIORITY APPLN. INFO.:			US 1989-403437 A	19890905
			US 1990-561537 A	19900806

OTHER SOURCE(S): MARPAT 115:136788
GI



I

II

AB Renin-inhibiting difluorodiol-containing peptides I [R = H, C1-7 alkyl, aryl, heterocyclyl, etc.; Z2 = CO, CHOH, NR2; R2 = H, C1-7 alkyl; Z3 = CO, CH2, NR2; Z4 = CH, COH, C(halo); Z1 = CHR1, C(:CHR7); R1 = C1-7 alkyl, cycloalkylalkyl, aralkyl, etc.; R7 = aryl, heterocyclyl; R3 = C1-7 alkyl, C2-7 alkenyl, hydroxyalkyl, etc.; R4 = C1-7 alkyl, cycloalkylmethyl, CH2Ph; Z5, Z6 = CHOH, CO; R8 = C1-7 alkyl, aryl, aralkyl, etc.; with provisos], useful also as antihypertensives, for example, were prepared Thus, 1 equiv N-methylmorpholine and 1 equiv ClCO2CH(Me)Et were added to a solution of BOC-Phe-Leu-OH in THF at -20°. The mixture was stirred 10 min and a solution of 2(S)-amino-1-cyclohexyl-4,4-difluoro-3(R),5(R)-dihydroxy-6-methylheptane (preparation given) in THF was added. The resulting solution was stirred 0.5 h, filtered and concentrated to give title compound

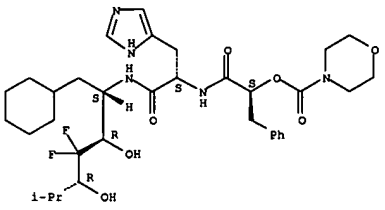
L6 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

(2S,3R,5R)-II. II had an IC50 of 0.64 nM against human renal renin.

IT **135934-08-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)

RN 135934-08-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-3,3-difluoro-2,4-dihydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,4S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

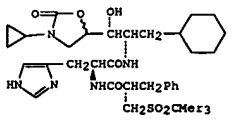


L6 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

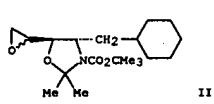
ACCESSION NUMBER: 1991:472226 CAPLUS
DOCUMENT NUMBER: 115:72226
TITLE: Amino acid derivatives
INVENTOR(S): Branca, Quirico; Neidhart, Werner; Ramuz, Henri; Stadler, Heinz; Wostl, Wolfgang
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 416373	A2	19910313	EP 1990-116088	19900822
EP 416373	A3	19920527		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2023099	AA	19910305	CA 1990-2023099	19900810
AU 9061360	A1	19910307	AU 1990-61360	19900827
AU 646640	B2	19940303		
ZA 9006856	A	19910626	ZA 1990-6856	19900828
HU 58060	A2	19920128	HU 1990-5676	19900829
JP 03099047	A2	19910424	JP 1990-228473	19900831
NO 9003832	A	19910305	NO 1990-3832	19900903
US 5688946	A	19971118	US 1994-277111	19940719
PRIORITY APPLN. INFO.:			CH 1989-3192 A	19890904
			CH 1990-2336 A	19900712
			US 1990-571689 B1	19900823

OTHER SOURCE(S): MARPAT 115:72226
GI



I



II

AB Amino acid derivs. RCONR1CH(CH2R2)CONHCHR3CHR4CR5R6R7 (R-R7 = substituents) were prepared for use as antihypertensives and renin inhibitors. Thus, amide I was prepared from epoxide II, H-His-OMe.2HCl, and (S)-PhCH2CH(CO2H)CH2SO2CMe3 in 5 steps. I had a renin-inhibiting ED50 of 0.0009 μM/L.

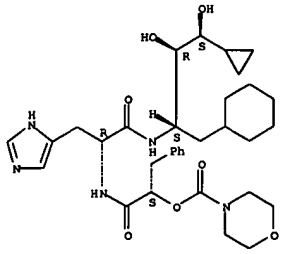
IT **134362-82-6P 134453-80-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 134362-82-6 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-3-cyclopropyl-

L6 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

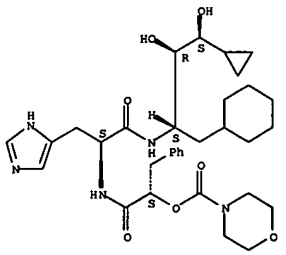
2,3-dihydroxypropyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[S*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 134453-80-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-3-cyclopropyl-2,3-dihydroxypropyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:450304 CAPLUS
DOCUMENT NUMBER: 115:50304
TITLE: Preparation of amino acid and peptide derivatives and related compounds as retroviral protease inhibitors
INVENTOR(S): Kempf, Dale J.; Norbeck, Daniel W.; Erickson, John W.; Codacovi, Lynn M.; Sham, Hing Leung; Plattner, Jacob J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Eur. Pat. Appl., 193 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 402646	A1	19901219	EP 1990-109319	19900517
EP 402646	B1	19980722		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5142056	A	19920825	US 1990-518730	19900509
EP 839798	A2	19980506	EP 1997-119700	19900517
EP 839798	A3	19981028		
EP 839798	B1	20050817		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 168677	E	19980815	AT 1990-109319	19900517
ES 2119737	T3	19981016	ES 1990-109319	19900517
AT 302180	E	20050915	AT 1997-119700	19900517
AU 9055711	A1	19901129	AU 1990-55711	19900518
AU 645493	B2	19940120		
IL 94444	A1	19990312	IL 1990-94444	19900520
CA 2017252	AA	19901123	CA 1990-2017252	19900522
CA 2017252	C	20010828		
JP 03128335	A2	19910531	JP 1990-133684	19900523
JP 2963910	B2	19991018		
US 5354866	A	19941011	US 1993-121673	19930914
US 5541334	A	19960730	US 1995-409380	19950323
US 5597926	A	19970128	US 1995-409767	19950323
US 5670675	A	19970923	US 1995-409365	19950323
US 5616714	A	19970401	US 1995-410260	19950324
US 5648497	A	19970715	US 1995-410623	19950324
US 5837873	A	19981117	US 1995-410162	19950324
US 5539122	A	19960723	US 1995-410996	19950327
US 5552558	A	19960903	US 1995-411032	19950327
US 5696270	A	19971209	US 1995-411140	19950327
US 5580984	A	19961203	US 1995-412253	19950328
US 5679797	A	19971021	US 1995-412244	19950328
US 5583232	A	19961210	US 1995-412821	19950329
US 5597927	A	19970128	US 1995-412438	19950329
US 5674882	A	19971007	US 1995-413136	19950329
US 5583233	A	19961210	US 1995-413290	19950330
US 5625072	A	19970429	US 1995-415827	19950403
US 5591860	A	19970107	US 1995-416272	19950404
US 5597928	A	19970128	US 1995-416607	19950404
US 5608072	A	19970304	US 1995-416259	19950404
US 5565418	A	19961015	US 1995-417304	19950405
US 5659044	A	19970819	US 1995-417165	19950405
US 5659045	A	19970819	US 1995-417295	19950405
US 5616720	A	19970401	US 1995-418056	19950406

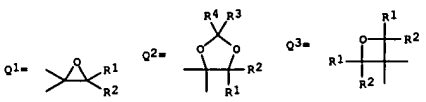
L6 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

US 5635523	A	19970603	US 1995-417879	19950406
US 5892052	A	19990406	US 1995-418031	19950406
US 5554783	A	19960910	US 1995-418978	19950407
US 5541206	A	19960730	US 1995-423387	19950425
HK 1012337	A1	20000505	HK 1998-113371	19981215
US 6531610	B1	20030311	US 2000-619785	20000720

PRIORITY APPLN. INFO.:

US 1989-355945	A	19890523
US 1989-405604	A	19890908
US 1989-456124	A	19891222
US 1990-518730	A	19900509
US 1983-355945	B2	19830523
EP 1990-109319	A3	19900517
US 1990-616170	B2	19901120
US 1991-746020	B2	19910815
US 1991-777626	A1	19911023
US 1992-880729	B1	19920508
US 1992-998114	B2	19921229
US 1993-164979	B1	19930207
US 1993-121673	A3	19930914
US 1993-158587	B3	19931202
US 1994-270210	A3	19940823
US 1994-358648	A3	19941219
US 1995-418031	A3	19950406
US 1998-207881	A3	19981208

OTHER SOURCE(S): MARPAT 115:50304
GI



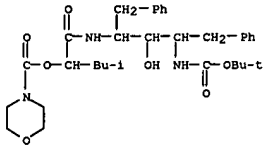
AB A-X-B [A,B = substituted amino, carbonyl, imino, alkyl, acyl, heterocyclyl, heterocyclylalkyl; X = CO, CHNR1R2, CHNHOR1, C(OH)CO2H, CH(OH), P(O)H, NOR1, SO, SO2, CH(OH)CHSH, CHSH, CH2SO2CH2, P(O)OR1, CH2SOCH2, Q1, Q2, Q3, etc.; R1,R2 = H, alkyl, hydroxyalkyl, alkoxyalkyl;

L6 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

R3,R4 = H, alkyl, alkoxyalkyl], were prepd. Thus, (2S,3R,4S,5S)-2,5-diamino-3,4-dihydroxy-1,6-diphenylhexane (prepn. given) in dioxane was treated with N-[(benzyloxycarbonylvalyl)oxy]succinimide (prepn. given) to give (2S,3R,4S,5S)-2,5-bis[(benzyloxycarbonylvalyl)amino]-3,4-dihydroxy-1,6-diphenylhexane. The latter inhibited HIV-1IIB in H9 cells with IC50 = 0.015-0.027 μM.

IT **134805-25-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as retroviral protease inhibitor)

RN 134805-25-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-4-phenyl-1-(phenylmethyl)butyl]amino]carbonyl]-3-methylbutyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:247790 CAPLUS
DOCUMENT NUMBER: 114:247790
TITLE: Preparation of peptide analogs as renin inhibitors
INVENTOR(S): Uchida, Itsuo; Shibata, Saizo; Yamada, Yasuki; Ikemoto, Yukinari; Iwata, Kunio; Ikegami, Kiyoteru; Nakamura, Ikuro
PATENT ASSIGNEE(S): Japan Tobacco, Inc., Japan; Yoshitomi Pharmaceutical Industries, Ltd.
SOURCE: Eur. Pat. Appl., 92 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 396065	A1	19901107	EP 1990-108163		19900428
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE					
CA 2015827	AA	19901102	CA 1990-2015827		19900501
JP 03204860	A2	19910906	JP 1990-111713		19900501
PRIORITY APPLN. INFO.:			JP 1989-112245	A	19890502
			JP 1989-278490	A	19891027

OTHER SOURCE(S): MARPAT 114:247790
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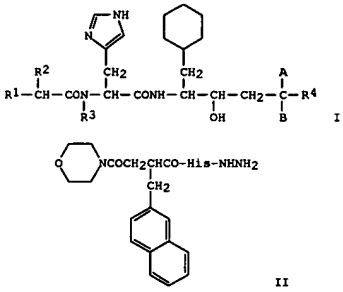
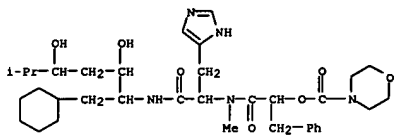


I

II

AB The title compds. [I; R1 = NH2, alkoxycarboxamido, morpholinocarbonylmethyl (Q), etc.; R2 = (substituted) aralkyl; R3 = H, alkyl; R4 = alkyl; A = OH and B = H, or AB = CO], were prepared 4 M HCl-dioxane and isopentyl nitrite were added sequentially to a solution of histidine hydrazide derivative II in DMF, the mixture was stirred 30 min at

L6 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
-20°, cooled to -30°, and neutralized with Et3N; 1-cyclohexyl-2-amino-3,5-dihydroxy-6-methylheptane in DMF was added, and the resulting mixt. was stirred at 0°for 48 h to give I [A = OH, R1 = Q, R2 = 2-naphthylmethyl, R3 = B = H, R4 = Me2CH]. The latter showed IC50 = 5.3 + 10-10 M against human renin.
IT 134018-11-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)
RN 134018-11-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2,4-dihydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]methylamino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)



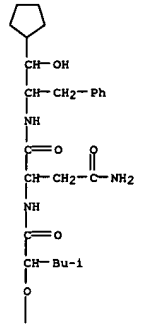
L6 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:247788 CAPLUS
DOCUMENT NUMBER: 114:247788
TITLE: Peptide derivatives preparation as retroviral protease inhibitors
INVENTOR(S): Kempf, Dale J.; Plattner, Jacob J.; Norbeck, Daniel W.; Boyd, Steven A.; Baker, William R.; Erickson, John W.; Fung, Anthony K. L.; Crowley, Steven R.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 8910752	A1	19891116	WO 1989-US2055		19890512
W: AU, DK, JP, KR, US					
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
EP 342541	A2	19891123	EP 1989-108590		19890512
EP 342541	A3	19911106			
R: ES, GR					
AU 8935660	A1	19891129	AU 1989-35660		19890512
EP 415981	A1	19910313	EP 1989-905856		19890512
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
JP 03504247	T2	19910919	JP 1989-506033		19890512
PRIORITY APPLN. INFO.:			US 1988-194678	A2	19880513
			WO 1989-US2055	A	19890512

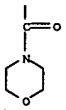
OTHER SOURCE(S): MARPAT 114:247788
AB Peptide derivs. are prepared as retroviral protease inhibitors. Synthetic processess involved carbodiimide coupling, or coupling in combination with deprotection, and reaction with mixed anhydrides. Thus, N-methyl-1-cyclohexenecarboxamide was treated with BuLi in THF, treated with ClTi(OPr-iso)3, and then Boc-phenylalaninal to give N-methyl-6-[2-(tert-butoxycarbonyl)amino-1-hydroxy-3-phenyl]propyl-1-cyclohexenecarboxamide. This was then deprotected with HCl in dioxane to give N-methyl-6-(2-amino-1-hydroxy-3-phenylpropyl)-1-cyclohexenecarboxamide-HCl (I). I was coupled with Boc-Leu-Asn in the presence of 1BO-BuO2CCl to give the amide.
IT 129776-69-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 129776-69-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[3-amino-1-[[[2-cyclopentyl-2-hydroxy-1-(phenylmethyl)ethyl]amino]carbonyl]-3-oxopropyl]amino]-1-(2-methylpropyl)-2-oxoethyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

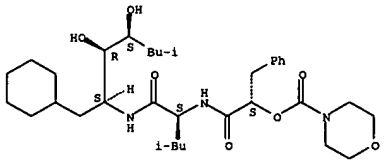


PAGE 2-A



L6 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:199052 CAPLUS
DOCUMENT NUMBER: 114:199052
TITLE: Orally active renin inhibitors containing a novel aminoglycol dipeptide (Leu-Val) mimetic
AUTHOR(S): Hanson, Gunnar J.; Baran, John S.; Clare, Michael; Williams, Kenneth; Babler, Maribeth; Bittner, Stephen E.; Russell, Mark A.; Papaioannou, S. E.; Yang, Po Chang; Walsh, Gerald M.
CORPORATE SOURCE: G.D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 11th (1990), Meeting Date 1989, 396-8. Editor(s): Rivier, Jean E.; Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.
CODEN: 56XTA7
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A discussion on structure activity relationship and modeling of SC-46944 complexation to endothiapepsin.
IT 120729-15-9, SC 46944
RL: BIOL (Biological study)
(endothiapepsin binding of, renin inhibition and structure in relation to)
RN 120729-15-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



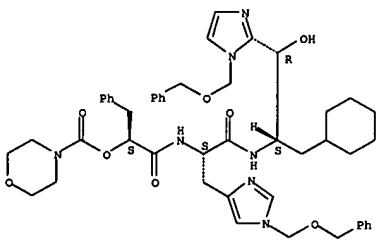
L6 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:459840 CAPLUS
DOCUMENT NUMBER: 113:59840
TITLE: Preparation of peptides as inhibitors of renin and viral protease
INVENTOR(S): Weller, Harold N., III; Ryono, Denis E.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 341481	A1	19891115	EP 1989-107378	19890424
R: DE, FR, GB, IT				
US 5151513	A	19920929	US 1988-187782	19880429
JP 02011575	A2	19900116	JP 1989-111916	19890428
PRIORITY APPLN. INFO.:			US 1988-187782 A	19880429

OTHER SOURCE(S): MARPAT 113:59840
AB XOCHR5CONHCHR4CONHCHR3CHR1OH [I; X = R6(CH2)mANR10CO, R6(CH2)mACO, etc.; R1 = (benzo-fused) 5- or 6-membered N-heterocyclyl; R3, R4, R5 = H, (halo)alkyl, aryl(alkyl), amino(alkyl), heterocyclyl(alkyl), hydroxy(alkyl), etc.; R6 = H, alkyl, aryl, pyridyl, cycloalkyl; R10 = R6, arylalkyl, pyridylalkyl, cycloalkylalkyl; m = 0-5; A = bond, CH(CH2)mR6], useful as renin inhibitors (no data), were prepared Thus, [S-2-(4-morpholinylcarbonyloxy)-1-oxo-3-phenylpropyl]-N-[1S,2R-1-cyclohexylmethyl-2-hydroxy-2-(1H-imidazol-2-yl)ethyl]-L-histidinamide was prepared in 18 steps starting from L-phenylalanine. I are said to also be
inhibitors of viral proteases and may be useful against retroviruses including HTLV-I and HTLV-III.
IT 128188-29-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for renin inhibitor and viral protease
inhibitor)
RN 128188-29-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-2-[1-[(phenylmethoxy)methyl]-1H-imidazol-2-yl]ethyl]amino]-2-oxo-1-[[1-[(phenylmethoxy)methyl]-1H-imidazol-4-yl]methyl]ethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*]]- (9CI) (CA INDEX NAME)

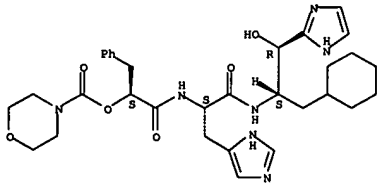
Absolute stereochemistry.

L6 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT 128188-25-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as renin inhibitor and viral protease inhibitor)
RN 128188-25-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-2-(1H-imidazol-2-yl)ethyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, dihydrochloride, [1S-[1R*[R*(R*)],2S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L6 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:669 CAPLUS
DOCUMENT NUMBER: 112:669
TITLE: Amino acid derivatives, processes for their preparation, and pharmaceutical compositions comprising them for treatment of hypertension and heart failure
INVENTOR(S): Hemmi, Keiji; Neya, Masahiro; Marusawa, Hiroshi; Imai,
Keisuke; Kayakiri, Natsuko; Hashimoto, Masashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 60 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 300189	A2	19890125	EP 1988-109430	19880614
EP 300189	A3	19900822		
EP 300189	B1	19941102		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8804087	A	19890222	ZA 1988-4087	19880608
US 4921855	A	19900501	US 1988-204549	19880609
ES 2067456	T3	19950401	ES 1988-109430	19880614
FI 8802875	A	19881223	FI 1988-2875	19880616
FI 96202	B	19960215		
FI 96202	C	19960527		
IL 86782	A1	19930404	IL 1988-86782	19880616
AU 8818190	A1	19881222	AU 1988-18190	19880621
AU 617674	B2	19911205		
DK 8803400	A	19881223	DK 1988-3400	19880621
NO 8802732	A	19881223	NO 1988-2732	19880621
NO 175371	B	19940627		
NO 175371	C	19941005		
CN 1030411	A	19890118	CN 1988-103878	19880621
CN 1026892	B	19941207		
JP 01019071	A2	19890123	JP 1988-153041	19880621
JP 06025147	B4	19940406		
HU 47917	A2	19890428	HU 1988-3164	19880621
HU 202212	B	19910228		
SU 1801107	A3	19930307	SU 1988-4356019	19880621
US 5142048	A	19920825	US 1990-462117	19900108
RU 2070195	C1	19961210	RU 1991-5010142	19911122
US 5223489	A	19930629	US 1992-828193	19920130
PRIORITY APPLN. INFO.:			GB 1987-14597 A	19870622
			GB 1987-25511 A	19871030
			GB 1988-5389 A	19880307
			US 1988-204549 A3	19880609
			US 1990-462117 A3	19900108

GI

L6 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

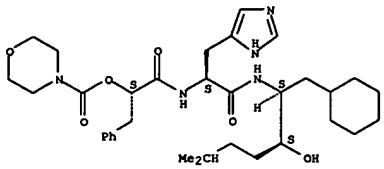
AB A process for preparing I [R1 = lower alkyl optionally substituted with acyl, hydroxy, lower alkoxy, aryl, lower alkylthio, NR5R6; R5 = H, acyl; R6 = H, lower alkyl, aryl, (lower alkyl- or acyl-substituted) amino; R2, R3 = H, lower alkyl; R4 = lower alkyl; R1NR2 = heterocycle optionally substituted with lower alkyl, hydroxy(lower)alkyl, lower alkoxy(lower)alkyl, acyl(lower)alkyl, oxo, acyl] or its pharmaceutically acceptable salt comprises (a) reacting II (R3, R4 as above; R8 = H, N-protective group) or its reactive derivative at the amino group or a salt thereof with III (R1, R2 as above) or its reactive derivative at the COO group or a salt thereof, and, if necessary, eliminating the N-protective group or (b) subjecting IV (R2, R3, R4, R6 as above; R7 = N-protective group; A = lower alkylene) or its salt to elimination reaction of R7 to give V (R2, R3, R4, R6, A as above) or its salt. I are useful as antihypertensives or for the treatment of heart failure. A solution of 2(S)-[N-(2-morpholinocarbonylethyl)-N-methylaminocarbonyloxy]-3-phenylpropionic acid (preparation described) 449 and 2(S)-(Nα-methyl-Nim-tosyl-L-histidyl)amino-1-cyclohexyl-3(S)-hydroxy-6-methylheptane (preparation described) 300 mg in CH2Cl2 (30 mL) was mixed with N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide-HCl 140 mg at 5° overnight. The residue was dissolved in EtOAc, washed with HCl/NaHCO3, dried, redissolved in DMF, and reacted with pyridine-HCl 650 mg for 2 h at room temperature Workup and purification by TLC yielded 2(S)-[Nα-[2(S)-[N-(2-morpholinocarbonylethyl)-N-methylaminocarbonyloxy]-3-phenylpropionyl]-Nα-methyl-L-histidyl]amino-1-cyclohexyl-3(S)-hydroxy-6-methylheptane (VI) 221 mg (m.p. 80-87°) as an amorphous powder. VI, dissolved in HCl and orally administered to Na-depleted male or female cynomolgus monkeys (32 mg/kg), reduced mean arterial blood pressure and plasma renin activity by 18 and 92%, resp.

IT **124072-32-8P 124072-33-9P 124076-21-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antihypertensive)

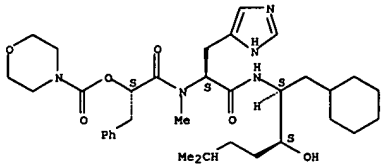
RN 124072-32-8 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



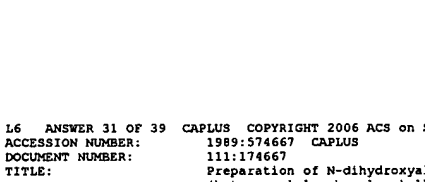
L6 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 124072-33-9 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]methylamino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2R*]]- (9CI) (CA INDEX NAME)

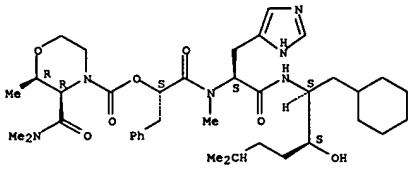
Absolute stereochemistry.



RN 124076-21-7 CAPLUS

CN 4-Morpholinecarboxylic acid, 3-[(dimethylamino)carbonyl]-2-methyl-, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]methylamino]-2-oxo-1-(phenylmethyl)ethyl ester, [2R-[2α,3α,4[S*[S*(1S*,2S*)]]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



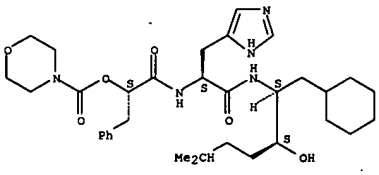
L6 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

IT **124072-32-8P 124072-33-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antihypertensive, renin inhibition in relation to)

RN 124072-32-8 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2R*]]- (9CI) (CA INDEX NAME)

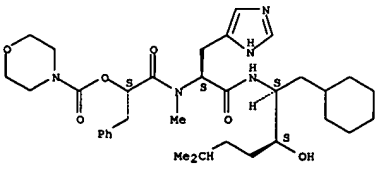
Absolute stereochemistry.



RN 124072-33-9 CAPLUS

CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]methylamino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:574667 CAPLUS
DOCUMENT NUMBER: 111:174667
TITLE: Preparation of N-dihydroxyalkyl-Nα-[(α-(heterocyclylcarbonyloxy)alkanoyl]-α-amino acid amides as antihypertensive agents
INVENTOR(S): Hanson, Gunnar James; Baran, John Stanislaus
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 310071	A2	19890405	EP 1988-116074	19880929
EP 310071	A3	19891129		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
US 4977141	A	19901211	US 1987-103625	19871001
JP 01113357	A2	19890502	JP 1988-247293	19880930
PRIORITY APPLN. INFO.:			US 1987-103625 A	19871001

OTHER SOURCE(S): CASREACT 111:174667; MARPAT 111:174667

GI For diagram(s), see printed CA Issue.

AB The title compds. [I; A = O, S; R1 = H, alkyl, haloalkyl, alkoxycarbonyl, etc.; R2 = alkyl, PhCH2; R3 = alkyl, acylaminoalkyl, naphthylmethyl, aryl, (substituted) PhCH2; R4, R5 = H, alkyl; R6 = (un)substituted cycloalkyl, Ph, cycloalkylalkyl, phenylalkyl; T = H, alkyl, alkoxy, etc.; X = cyclic imino groups Q1-Q3, NR7R8; Q, Y = CH2, CHOR9, O, S, SO, SO2, NR10; R9 = H, alkyl; R10 = H, Ph, COR11; R11 = H, alkyl; a-d = 0-3; m, n = 1-4; p = 1-3; r, t-v = 0-2] were prepared (2R,3S)-RNHCH(CH2Ph)CH(OAc)CHO (R = BOC = Me3CO2C) (preparation given) was stirred 2 h with Me2CHCH2MgCl in THF and the product, after hydrolysis, was hydrogenated over Rh/C to give (2S,3R,4S)-RNHCH(CH2R6)[CH(OH)]2CH2CHMe2 (II; R = BOC, R6 = cyclohexyl) which was deprotected and condensed with L-Me2CHCH2CH(NHBOC)CO2CO2CH2CHMe2 (prepared from BOC-L-leucine and ClCO2CH2CHMe2) to give, after deprotection, the L-leucinamide of II (R = H, R6 = cyclohexyl). The latter was added to O-(morpholinocarbonyl)-3-L-lactic acid which had been treated with ClCO2CH2CMe2 in CH2Cl2 and the whole maintained 8 h at 0° to give the N'-[O-(morpholinocarbonyl)-3-L-phenyllactyl]-L-leucineamide of II (R = H, R6 = cyclohexyl) which had ED50 of 0.012 mg/kg i.v. for reduction of plasma renin activity in Rhesus monkeys.

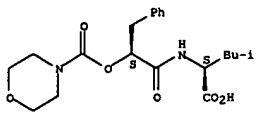
IT **122994-25-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of antihypertensives)

RN 122994-25-6 CAPLUS

CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-carboxy-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

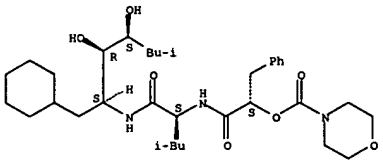
L6 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



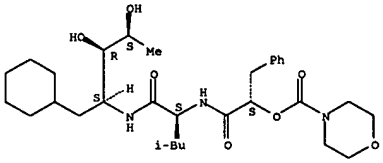
IT **120729-15-9P 122994-22-3P 122994-23-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antihypertensive)
RN 120729-15-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 122994-22-3 CAPLUS
CN L-Arabinitol, 1-cyclohexyl-1,2,5-trideoxy-2-[[(2S)-4-methyl-2-[[(2S)-2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]amino]-1-oxopentyl]amino]- (9CI) (CA INDEX NAME)

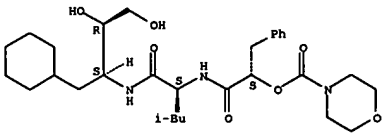
Absolute stereochemistry.



L6 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 122994-23-4 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R)-1-(cyclohexylmethyl)-2,3-dihydroxypropyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

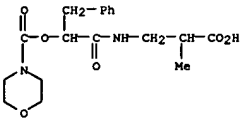
ACCESSION NUMBER: 1989:534757 CAPLUS
DOCUMENT NUMBER: 111:134757
TITLE: Preparation and testing of aminocyclohexyldihydroxyalkane phenyllactyl-β-alaninamides as renin inhibitors
INVENTOR(S): Hanson, Gunnar James; Baran, John Stanislaus
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 310073	A2	19890405	EP 1988-116077	19880929
EP 310073	A3	19891129		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
US 5089471	A	19920218	US 1987-103632	19871001
JP 01113356	A2	19890502	JP 1988-247291	19880930
PRIORITY APPLN. INFO.:			US 1987-103632 A	19871001

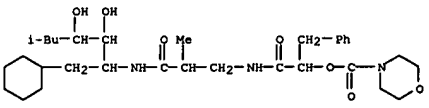
OTHER SOURCE(S): MARPAT 111:134757
GI For diagram(s), see printed CA Issue.
AB The title compds [I; R1 = H, alkyl, haloalkyl, alkylcycloalkyl, alkoxycarbonyl, alkylcycloalkenyl; R2 = alkyl, imidazolemethyl, PhCH2; R3 = alkyl, acylaminoalkyl, naphthylmethyl, aryl, (substituted) PhCH2; R4, R5 = H, alkyl; R6 = H, Ph; R7 = (substituted) cycloalkyl, Ph, cycloalkylalkyl, phenylalkyl; R8, R9 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, Ph, PhCH2, naphthyl, naphthylmethyl; A = O, S; T = H, alkyl, alkoxy, oxo, halo, haloalkyl, alkenyl, alkynyl, cyano; X = Q1, Q2, R8R9N, Y = CH2, CH(OH), alkoxymethylene, O, S, SO, SO2, imino; a -d = 0-3; m, n = 1-4], useful as renin inhibitors, were prepared O-(N-Morpholinocarbonyl)-3-L-phenyllactic acid (preparation from L-3-phenyllactic acid given) in CH2Cl2 containing N-methylpiperidine at -10° was treated with iso-Bu chloroformate and then D,L-α-methyl-β-alanine Me ester hydrochloride and N-methylpiperidine in CH2Cl2. The mixture was stirred 2 h at -10° and 16 h at room temp to give 57% O-(N-morpholinocarbonyl)-3L-phenyllactyl-DL-α-methyl-β-alanine. The latter and N-methylpiperidine in CH2Cl2 at -10° was treated with iso-Bu chloroformate and then 2S,3R,4S-2-amino-1-cyclohexyl-3,4-dihydroxy-6-methylheptane (preparation given) in CH2Cl2. The mixture was stirred for 3 h at -10° to give the O-(N-morpholinocarbonyl)-3L-phenyllactyl-DL-α-methyl-β-alaninamide of 2S,3R,4S-2-amino-1-cyclohexyl-3,4-dihydroxy-6-methylheptane. The latter inhibited human renin with an IC50 of 2.8 + 10-7M.

IT **122579-05-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for renin inhibitor)
RN 122579-05-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(2-carboxypropyl)amino)-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

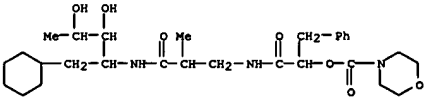
L6 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT **122579-01-5P 122579-02-6P 122579-03-7P**
122621-75-4P 122621-76-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)
RN 122579-01-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[3-[[1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-2-methyl-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

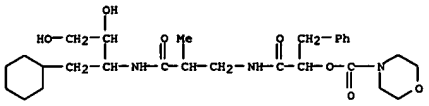


RN 122579-02-6 CAPLUS
CN Pentitol, 5-cyclohexyl-1,4,5-trideoxy-4-[[2-methyl-3-[[2-[(4-morpholinylcarbonyl)oxy]-1-oxo-3-phenylpropyl]amino]propyl]amino]- (9CI) (CA INDEX NAME)



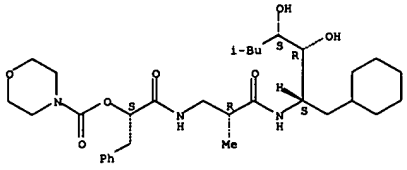
RN 122579-03-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[3-[[1-(cyclohexylmethyl)-2,3-dihydroxypropyl]amino]-2-methyl-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



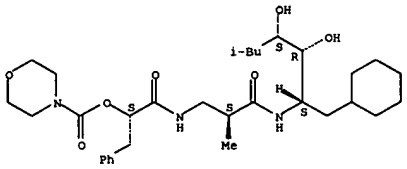
RN 122621-75-4 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(2R)-3-[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-2-methyl-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



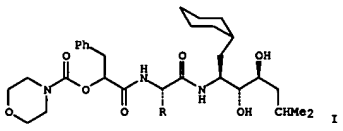
RN 122621-76-5 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(2S)-3-[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-2-methyl-3-oxopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:225010 CAPLUS
DOCUMENT NUMBER: 110:225010
TITLE: A new class of orally active glycol renin inhibitors containing phenyllactic acid at P3
AUTHOR(S): Hanson, Gunnar J.; Baran, John S.; Lowrie, Harman S.; Russell, Mark A.; Sarussi, Steven J.; Williams, Kenneth; Babler, Maribeth; Bittner, Stephen E.; Papaioannou, S. E.; et al.
CORPORATE SOURCE: G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Biochemical and Biophysical Research Communications (1989), 160(1), 1-5
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



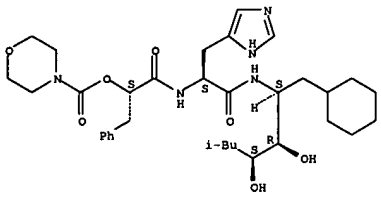
AB A new series of renin inhibitors based on dipeptide glycols, replacing the P4-P3 subsites with an O-(N-morpholinocarbonyl)-3-L-phenyllactic acid residue I (R = iso-Bu, CH2-imidazole, etc.) was tested. This modification proved bioisosteric with Boc-L-phenylalanine, giving rise to highly potent human renin inhibitors (1-5 nM), e.g., SC-46944 (IC50 = 5 nM). Moreover, this change produced compds. that are orally efficacious in reducing plasma renin activity in salt-depleted marmosets.

IT **114457-15-7**, SC 47563 **120729-15-9**, SC 46944 **120768-80-1**, SC 47557 **120850-29-5**, SC 48272
RL: BIOL (Biological study)
(renin inhibition by, structure in relation to, in humans and laboratory animals)

RN 114457-15-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

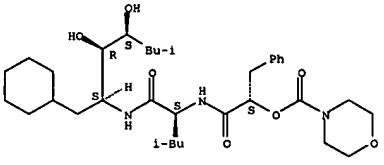
Absolute stereochemistry.

L6 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 120729-15-9 CAPLUS
CN 4-Morpholinecarboxylic acid, (1S)-2-[[(1S)-1-[[[(1S,2R,3S)-1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester (9CI) (CA INDEX NAME)

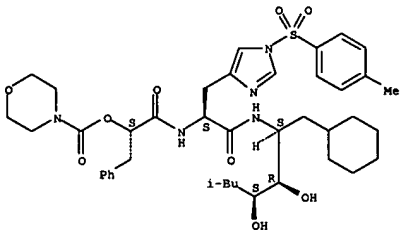
Absolute stereochemistry.



RN 120768-80-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-1-[[1-[(4-methylphenyl)sulfonyl]-1H-imidazol-4-yl]methyl]-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

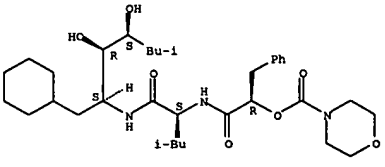
Absolute stereochemistry.

L6 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 120850-29-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-[[[1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]carbonyl]-3-methylbutyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(S*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:154889 CAPLUS
DOCUMENT NUMBER: 110:154889
TITLE: Preparation of norstatine- and norcyclostatine-containing peptides as renin inhibitors
INVENTOR(S): Hoover, Dennis Jay; Wester, Ronald Thure; Rosati, Robert Louis
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 86 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

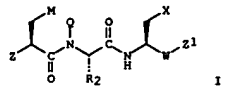
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 266950	A2	19880511	EP 1987-309461	19871027
EP 266950	A3	19900411		
EP 266950	B1	19931229		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IN 172976	A	19940115	IN 1987-DE905	19871015
CN 87101499	A	19880511	CN 1987-101499	19871023
CN 1027271	B	19950104		
US 4814342	A	19890321	US 1987-112976	19871023
AT 99324	E	19940115	AT 1987-309461	19871027
ES 2061512	T3	19941216	ES 1987-309461	19871027
CA 1310793	A1	19921124	CA 1987-550413	19871028
DK 8705684	A	19880501	DK 1987-5684	19871030
FI 8704787	A	19880501	FI 1987-4787	19871030
FI 90346	B	19931015		
FI 90346	C	19940125		
NO 8704530	A	19880502	NO 1987-4530	19871030
NO 173017	B	19930705		
NO 173017	C	19931013		
AU 8780541	A1	19880505	AU 1987-80541	19871030
AU 585180	B2	19890608		
HU 45270	A2	19880628	HU 1987-4901	19871030
HU 207869	B	19930628		
JP 63183551	A2	19880728	JP 1987-275583	19871030
DD 262583	A5	19881207	DD 1987-308473	19871030
ZA 8708158	A	19890628	ZA 1987-8158	19871030
SU 1706391	A3	19920115	SU 1987-4203604	19871030
US 4935405	A	19900619	US 1988-277614	19881129
US 5034376	A	19910723	US 1990-497041	19900321
IN 175148	A	19950506	IN 1990-DE781	19900803
JP 07173134	A2	19950711	JP 1994-221930	19940916
JP 07108901	B4	19951122		

PRIORITY APPLN. INFO.: US 1986-925449 A 19861031
US 1987-68982 A 19870701
IN 1987-DE905 A1 19871015
US 1987-112976 A3 19871023
EP 1987-309461 A 19871027
US 1988-277614 A3 19881129

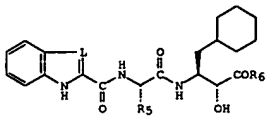
OTHER SOURCE(S): CASREACT 110:154889; MARPAT 110:154889

L6 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

GI



I



II

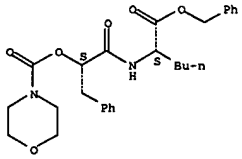
AB The title peptides (I, II; Z = R1-Ym-Ap; R1 = C1-6 alkyl, C1-4 alkoxy, (un) substituted amino, morpholino, piperidyl, piperazino, (substituted)piperidino, thiomorpholino, pyridyl, etc; Y = CO, P(O)OMe, SO2; A = NMe, NH, O; m, p = 0, 1; M = Ph, PhCH2, naphthyl, thienyl, MeOC6H4, ClC6H4, HOC6H4, C6-7 cycloalkyl; X = Me, H; R2 = C1-5 alkyl, substituted C1-2 alkyl, PhCH2, guanidino-C1-3 alkyl, 4-aminobutyl, imidazol-4-ylmethyl, etc.; X = cyclohexyl, Me2CH, Ph; W = CHOH, CO, CHN3, CHNH2, CMeOH, etc.; Z1 = CH2OH, R-X1-T; R = CO; X1 = O, NH, NMe, CH2, bond; T = C1-5 alkyl, C1-4 hydroxyalkyl, C1-4 alkylcarbamoyl, H, trifluoroethyl, Ph, PhCH2, morpholino, etc.; L = CH, N; R5 = imidazol-4-ylmethyl, C2-5 alkyl; R6 = C1-4 alkoxy, C1-4 alkylamino; provided that when m = O, P = O; when A = O, Y = CO; when T = C1-4 alkylcaRbamoyl, X1 = NH, NMe, CH2; when T = C2-5 alkylamino, C1-2 alkoxyamino, morpholino or 4-C1-2 alkylpiperazino, X1 = CH2, bond], useful as antihypertensives (no data), were prepared Treatment of (S)-3-(tert-butoxycarbonylamino)-4-cyclohexyl-(R)-2-hydroxybutyric acid with Me2CHCH2O2CCl in THF containing Et3N and amidation of the resulting mixed anhydride with MeNH2 gave 42% N-methyl-3-(tert-butoxycarbonylamino)-4-cyclohexyl-(R)-2-hydroxybutyramide (BOC-nor-C-Sta-NHMe). Deprotection of the latter with 4N HCl in dioxane, followed by peptide coupling with BOC-Phe-His(imBOC)-OH (BOC = CO2CMe3) in CH2Cl2 in the presence of Et3N, hydroxybenzotriazole, and DCC, gave BOC-Phe-His(imBOC)-nor-C-Sta-NHMe, which was treated with AcOH-H2O(80:20) to give BOC-Phe-His-nor-C-Sta-NHMe.

IT **119642-75-0P 119642-76-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for renin-inhibiting antihypertensive)

RN 119642-75-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-oxo-2-[[1-[(phenylmethoxy)carbonyl]pentyl]amino]-1-(phenylmethyl)ethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

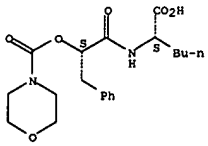
Absolute stereochemistry.

L6 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 119642-76-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[(1-carboxypentyl)amino]-2-oxo-1-(phenylmethyl)ethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

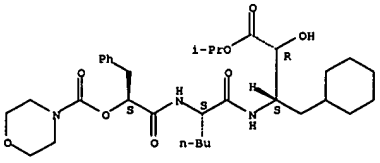
Absolute stereochemistry.



IT **119624-90-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin-inhibiting antihypertensive)

RN 119624-90-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[1-[[[1-(cyclohexylmethyl)-2-hydroxy-3-(1-methylethoxy)-3-oxopropyl]amino]carbonyl]pentyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN

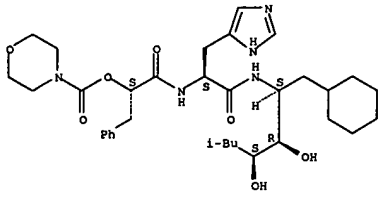
ACCESSION NUMBER: 1989:135731 CAPLUS
DOCUMENT NUMBER: 110:135731
TITLE: Preparation and testing of peptidylaminodiols as renin inhibitors
INVENTOR(S): Fung, Anthony K. L.; Kempf, Dale John; Luly, Jay Richard; Rosenberg, Saul Howard; Plattner, Jacob John
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8805050	A1	19880714	WO 1987-US3376	19871222
W: AU, DK, JP, KR				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
IL 97441	A1	19920906	IL 1987-97441	19870112
US 5032577	A	19910716	US 1987-132356	19871218
AU 8811580	A1	19880727	AU 1988-11580	19871222
AU 609774	B2	19910509		
EP 295294	A1	19881221	EP 1988-900918	19871222
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 01502514	T2	19890831	JP 1988-501082	19871222
IL 84945	A1	19920216	IL 1987-84945	19871225
US 4845079	A	19890704	US 1988-217106	19880711
DK 8804834	A	19880830	DK 1988-4834	19880830
CA 1307289	A2	19920908	CA 1991-615975	19910108
AU 9170281	A1	19910418	AU 1991-70281	19910205
AU 638093	B2	19930617		
US 5091575	A	19920225	US 1991-713644	19910610
US 5214129	A	19930525	US 1991-793773	19911118

PRIORITY APPLN. INFO.: US 1986-943567 A 19861231
US 1987-132356 A 19871218
US 1985-693951 B2 19850123
US 1986-818714 A 19860116
US 1986-818715 A 19860116
US 1986-818734 A 19860116
US 1986-895009 A 19860807
IL 1987-81234 A 19870112
CA 1987-527514 A3 19870116
WO 1987-US3376 A 19871222
US 1988-217106 A3 19880711
US 1989-327467 B1 19890322
US 1991-713644 A3 19910610

L6 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
OTHER SOURCE(S): MARPAT 110:135731
AB ACHR1-W-U-CHR3CONHCHR4CR5R8CR6R7R9 [I; A = (un)substituted amino, acylamino, etc.; W = CO, CHOH; U = CH2, NR2; R1 = alkyl, cycloalkylmethyl, (substituted) PhCH2, anilino, thiophenoxy, etc.; R2, R7 = H, alkyl; R3 = alkyl, alkenyl, alkoxyalkoxyalkyl, PhCH2, heterocyclylmethyl; R4 = alkyl, cycloalkylmethyl, PhCH2; R5 = H, CH2:CH, HCO, HOCH2; R6 = H, alkyl, CH2:CH, arylalkyl; R8, R9 = OH, NH2], useful as renin inhibitors, were prepared 2S-tert-Butyloxycarbonylamino-1-cyclohexylbut-3-ene (preparation given) was deprotected with HCl/MeOH and coupled with BOC-Phe-Ala-OH (BOC = CO2CMe3), using iso-Bu chloroformate and N-methylmorpholine in THF/DMF at -13°. the product was treated with OsO4/N-methylmorpholine N-oxide in THF to give 3S-N-(tert-butoxycarbonylphenylalanylalanylamino)-4-cyclohexyl-1,2(R,S)-dihydroxybutane. I inhibited renin with IC50's of 0.3-4000 nM.
IT **114457-15-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)
RN 114457-15-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



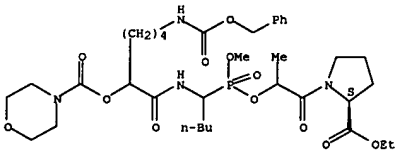
L6 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:76063 CAPLUS
DOCUMENT NUMBER: 110:76063
TITLE: Preparation of [[(aminoalkanoyl)amino]alkyl]phosphonat es as angiotensin-converting enzyme inhibitors
INVENTOR(S): Loots, Melanie Jane; Karanewsky, Donald Steven
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 82 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 249445	A2	19871216	EP 1987-305099	19870609
EP 249445	A3	19890906		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4849414	A	19890718	US 1987-52100	19870520
CA 1307787	A1	19920922	CA 1987-538351	19870529
ZA 8703984	A	19880127	ZA 1987-3984	19870603
DK 8702958	A	19871212	DK 1987-2958	19870610
AU 8774094	A1	19871217	AU 1987-74094	19870610
AU 593111	B2	19900201		
HU 45073	A2	19880530	HU 1987-2656	19870610
HU 198077	B	19890728		
JP 62292788	A2	19871219	JP 1987-147813	19870611
PRIORITY APPLN. INFO.:			US 1986-873035 A	19860611

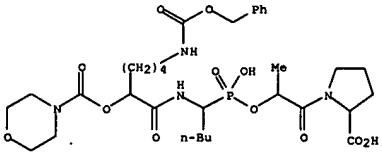
OTHER SOURCE(S): CASREACT 110:76063; MARPAT 110:76063
AB RCHR4CONHCHR2(CH2)nP(O)(OR3)OCHR1COX [I; R = NH2, NHCOR5, NHCO2R6, O2CR5; R5 = H, lower alkyl, phenylalkyl, furanylalkyl, pyridylalkyl, thienylalkyl, (un)substituted NH2, etc.; R6 = lower alkyl, cycloalkylalkyl, furanylalkyl, phenylalkyl, pyridylalkyl, thienylalkyl; R1, R4 = H, lower alkyl, CF3, (CH2)rR7; R7 = Cl, Br, F, Ph, C6H4OH-p, C6H4(OH)2-3,4, 3-indolyl, 4-imidazolyl, NH2, SH, NHC(:NH)NH2, CONH2, etc.; r = 1-7; n = 0, 1; R2 = lower alkyl, (CH2)rR8; R8 = (un)substituted Ph, cycloalkyl, NH2; R3 = H, lower alkyl, alkali or alkaline earth metal, etc.; X = an L-amino or imino acid or ester represented by 23 Markush formulas], useful as angiotensin-converting enzyme inhibitors (no data), were prepared
Condensation of Ph2CHNH2.H2P(O)OH with valeraldehyde and N-deprotection of the product with CF3CO2H/anisole, followed by acylation with PhCH2O2CCl, gave ZNH(CH2)5PH(O)OH (Z = PhCH2O2C) which was condensed with (S)-HOCHMeCO-Pro-OCH2Ph (preparation given) in THF in the presence of dicyclohexylcarbodiimide and 4-(dimethylamino)pyridine to give, after NaIO4 oxidation, (2S)-ZNH(CH2)5P(O)(OH)OCHMeCO-Pro-OCH2Ph. Hydrogenolysis of the latter over Pd(OH)2 on C gave (2S)-H2N(CH2)5P(O)(OH)OCHMeCo-Pro-OH which was persilylated with CF3CON(SiMe3)2 and then underwent amidation with R9-Lys(Z)-OH (R9 = cyclobutylcarbonyl) in THF containing N-methylmorpholine to give (S)-R9-Lys(Z)-NH(CH2)5P(O)(OH)OCHMeCO-Pro-OH, which was hydrogenolyzed over 10% Pd/C to give (S)-R9-Lys-NH(CH2)5P(O)(OH)OCHMeCO-Pro-OH) (II). Tablets were prepared each containing II 10, cornstarch 50, gelatin 7.5, Avicel 25, and Mg stearate 2.5 mg.

L6 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT **118602-58-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and demethylation of)
RN 118602-58-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-[[2-[2-(ethoxycarbonyl)-1-pyrrolidinyl]-1-methyl-2-oxoethoxy]methoxyphosphinyl]pentyl]amino]carbonyl]-5-[[(phenylmethoxy)carbonyl]amino]pentyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

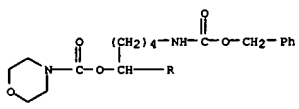


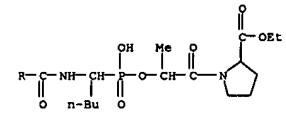
IT **118602-60-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)
RN 118602-60-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-[[2-(2-carboxy-1-pyrrolidinyl)-1-methyl-2-oxoethoxy]hydroxyphosphinyl]pentyl]amino]carbonyl]-5-[[(phenylmethoxy)carbonyl]amino]pentyl ester (9CI) (CA INDEX NAME)



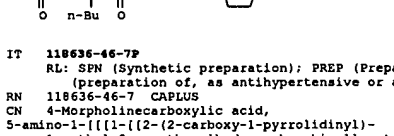
IT **118602-59-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
RN 118602-59-8 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-[[2-[2-(ethoxycarbonyl)-1-pyrrolidinyl]-1-methyl-2-oxoethoxy]hydroxyphosphinyl]pentyl]amino]carbonyl]-5-[[(phenylmethoxy)carbonyl]amino]pentyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)





IT **118636-46-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antihypertensive or analgesic)
RN 118636-46-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 5-amino-1-[[[1-[[2-(2-carboxy-1-pyrrolidinyl)-1-methyl-2-oxoethoxy]hydroxyphosphinyl]pentyl]amino]carbonyl]pentyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:24311 CAPLUS
DOCUMENT NUMBER: 110:24311
TITLE: Preparation and testing of peptidylaminodiols as renin inhibitors
INVENTOR(S): Luly, Jay Richard; Kempf, Dale John; Plattner, Jacob John
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

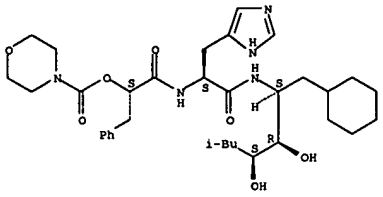
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 229667	A2	19870722	EP 1987-100424	19870115
EP 229667	A3	19910313		
EP 229667	B1	19940713		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 81234	A1	19920906	IL 1987-81234	19870112
IL 97441	A1	19920906	IL 1987-97441	19870112
DK 8700209	A	19870717	DK 1987-209	19870115
AU 8767599	A1	19870723	AU 1987-67599	19870115
AU 603080	B2	19901108		
ES 2059313	T3	19941116	ES 1987-100424	19870115
JP 62234052	A2	19871014	JP 1987-6280	19870116
JP 2525732	B2	19960821		
CA 1340940	A1	20000404	CA 1987-527514	19870116
CA 1340948	A1	20000404	CA 1987-615759	19870116
US 4845079	A	19890704	US 1988-217106	19880711
CA 1307289	A2	19920908	CA 1991-615975	19910108
AU 9170281	A1	19910418	AU 1991-70281	19910205
AU 638093	B2	19930617		
US 5091575	A	19920225	US 1991-713644	19910610
US 5214129	A	19930525	US 1991-793773	19911118
JP 06239811	A2	19940830	JP 1993-129480	19930531
JP 08000798	B4	19960110		

PRIORITY APPLN. INFO.:

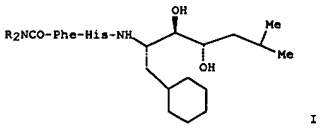
US 1986-818734	A	19860116
US 1986-895009	A	19860807
US 1986-943567	A	19861231
US 1985-693951	A2	19850123
US 1986-818714	A	19860116
US 1986-818715	A	19860116
IL 1987-81234	A	19870112
CA 1987-527514	A3	19870116
US 1988-217106	A3	19880711
US 1989-327467	B1	19890322
US 1991-713644	A3	19910610

L6 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
OTHER SOURCE(S): MARPAT 110:24311
AB AR1CHWUCHR3CONHCHR4CR5R8CR6R7R9 (I; A = H, OH, alkyl, alkoxy, thioalkoxy, amino, acylheterocyclyl, etc.; W = CO, CHOH; U = CH2, NR2; R2 = alkyl, cycloalkylmethyl, PhCH2, PhO, PhS, 2-naphthylmethyl, etc.; R2 = H, alkyl; R3 = alkyl, alkenyl, PhCH2, etc.; R4 = alkyl, cycloalkylmethyl, PhCH2; R5 = CH2:CH, CHO, CH2OH, H; R6 = H, alkyl, CH2:CH, arylalkyl; R7 = H, alkyl; R8, R9 = OH, NH2) were prepared as renin inhibitors useful for treatment of hypertension. BOC-Phe-His-OH was coupled with 2(S)-amino-1-cyclohexyl-3(R),4(S)-dihydroxy-6-methylheptane using dicyclohexylcarbodiimde/1-hydroxybenzotriazole to give 40-60% of the corresponding amide, which inhibited human renin with an IC50 of 1.5 nM.
IT 114457-15-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)
RN 114457-15-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:24298 CAPLUS
DOCUMENT NUMBER: 110:24298
TITLE: Renin inhibitors. Dipeptide analogs of angiotensinogen utilizing a structurally modified phenylalanine residue to impart proteolytic stability
AUTHOR(S): Plattner, Jacob J.; Marcotte, Patrick A.; Kleinert, Hollis D.; Stein, Herman H.; Greer, Jonathan; Bolis, Giorgio; Fung, Anthony K. L.; Bopp, Barbara A.; Luly, Jay R.; et al.
CORPORATE SOURCE: Pharm. Discovery Div., Abbott Lab., Abbott Park, IL, 60064, USA
SOURCE: Journal of Medicinal Chemistry (1988), 31(12), 2277-88
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:24298
GI

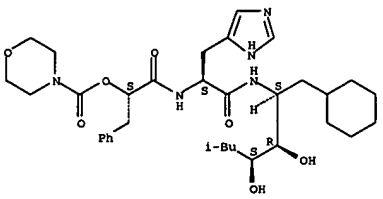


I

AB Title analogs, e.g. I (R = Me; NR2 = 4-hydroxypiperidino, 1-piperazinyl, morpholino), were prepared and evaluated for their susceptibility to cleavage by chymotrypsin. The compds. were designed by consideration of the structural requirements in the active-site region of renin and chymotrypsin. By systematic alteration of the P3 phenylalanine residue, compds. with varying degrees of renin-inhibitory potency and chymotrypsin susceptibility were obtained. Selected analogs from this group were examined in vivo for both their hypotensive effects and metabolic patterns.
IT 114457-15-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, renin-inhibiting activity, and chymotrypsin susceptibility of)
RN 114457-15-7 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-[[2-[[1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl]amino]-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl ester, [1S-[1R*[R*(R*)],2S*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

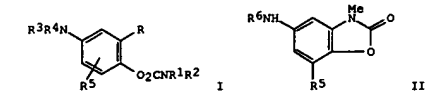
L6 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



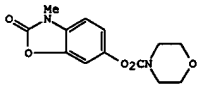
L6 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:217485 CAPLUS
DOCUMENT NUMBER: 96:217485
TITLE: Analgesic phenyl carbamates
PATENT ASSIGNEE(S): Kyoto Pharmaceutical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 57007459	A2	19820114	JP 1980-80783		19800613
PRIORITY APPLN. INFO.:			JP 1980-80783	A	19800613

OTHER SOURCE(S): CASREACT 96:217485
GI


I

II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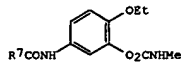
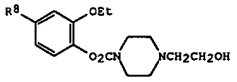

IV


V

AB Ninety-eight Ph carbamates I (R = H, OEt, Me, OCH2CH2NMe2, nicotinoyloxy; NR1R2 = NH2, NHMe, NMe2, morpholino, 4-methyl-1-piperazinyl, etc.; R3R4N = AcNH, MeSO2NH, Me2NCH2CONH, Me2NCOCH2NAc, 3-methyl-5-oxoimidazolidin-1-yl, etc.; R5 = H, 3-, 5-, or 6-Me), II (R5 = H, OEt; R6 = Me2NCH2CO, MeSO2, p-isobutyl-α-methylphenylacetyl, HOCH2CO), III, and IV (R7 = Me, 3-pyridyl), having analgesic activity comparable to aminopyrine and low toxicity in mice, were prepared Thus, reaction of 2,4-EtO(O2N)C6H3OH in aqueous NaOH with 30% COCl2 in PhMe at -5 to 0° gave the chloroformate, which was treated with N-(2-hydroxyethyl)piperazine to give V (R8 = NO2), which was hydrogenated to V (R8 = NH2), acylation of which with MeSO2Cl gave I [R = OEt, NR1R2 = 4-(2-hydroxyethyl)-1-piperazinyl, R3R4N = MeSO2NH, R5 = H].

L6 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 81934-83-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic activity of)
RN 81934-83-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 2-ethoxy-4-[[[(4-morpholinylcarbonyl)oxy]acetyl]amino]phenyl ester (9CI) (CA INDEX NAME)